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ARTICLE

Pharmacy in Serbia: The life and work of a distinguished pharmacist, Velimir Karić (1859-1946)

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Abstract

This article describes the transition of pharmacy in Serbia during the late nineteenth and early twentieth centuries, by examining the life and work of the pharmacist Velimir Karić. He was the owner of the first pharmacy in southern Serbia when a concession-based system operated for the opening of new pharmacies. With restrictions on pharmacy openings, conflict developed between pharmacists holding masters degrees and those who had passed the licence examination. Concessions were originally awarded by a general Chamber of Commerce, but the Serbian Pharmaceutical Society pressed successfully for a separate pharmacy Chamber. Difficulties in maintaining drug supplies at times of war led to the creation of a Pharmacy Buying Consortium. Central to all these developments was Velimir Karić, who as well as being president of the Serbian Pharmaceutical Society was a national deputy and a philanthropist.

Introduction: A brief history of Serbia

Serbia is a country with a long history, much of which has been dominated by conflict with its neighbours. Slavs had settled in the Balkans as early as the sixth and seventh centuries, resulting in the First Serbian Principality of the Vlastimirović.[1] This evolved into a Grand Principality during the eleventh century, and in 1217 the Kingdom of Serbia was established under the Nemanjić. In 1345 a Serbian Empire was established, spanning a large part of the Balkans.

In 1459, a Serbian despotate was conquered by the Turks. At the beginning of the nineteenth century, in 1804, the Serbian revolution against the Ottoman rule in Serbia began. The fight against the Turks resulted in Serbia gaining independence at the 1878 Berlin Congress. In 1882, the Principality of Serbia became a Kingdom during the reign of Milan Obrenovic.[2]

At the conclusion of these wars Serbia succeeded in extending its territory, winning the right to rule over four southern Morava districts in the towns of Niš, Pirot, Toplica and Vranje, where about 300,000 people lived.[3] Recognition by the Great Powers came through the Congress of Berlin, which took place in the summer of 1878. Within the boundaries set in 1878, Serbia (which between 1882 and 1918 was known as the Kingdom of Serbia) carried on its development until 1912, when war broke out with its neighbours.

Serbia was the victor in the Balkan Wars of 1912-1913, and regained Vardar Macedonia, Kosovo and Raška (Old Serbia), but again found itself at the centre of things during the First World War. At its end in 1918, the region of Vojvodina proclaimed its secession from the Austro-Hungarian Empire in order to unite with the pan-Slavic State of Slovenes, Croats and Serbs. The Kingdom of Serbia joined the union on 1 December 1918, and the country was named the Kingdom of Serbs, Croats and Slovenes.

Serbia achieved its current borders at the end of the Second World War, when it became part of the Federal People's Republic of Yugoslavia, which was proclaimed in November 1945. Following the breakup of the Federal Republic of Yugoslavia after a series of wars in the 1990s, Serbia became an independent state again on 5 June 2006, following the ending of a short-lived union with Montenegro.

Pharmacy in Serbia from 1830

Pharmacy too has a long history in Serbia, having developed over several centuries. The first pharmacy in Serbia was established during the reign of Prince Miloš Obrenović in 1830, by the pharmacist Mateja Ivanovic, while the northern part of Serbia was still under Austro-Hungarian domination.[4, 5] In this region, pharmacies were established from 1839, but they were organized and run under Austro-Hungarian rules. In the third decade of the nineteenth century, the Principality of Serbia – which continued until 1882 – set the foundations of an organized system of public health care. When the Turks left Serbia in 1867, a new era commenced regarding its demographic, cultural and health evolution; this heralded significant developments in the profession of pharmacy.

By the mid-nineteenth century a concession system operated with regard to the opening of new pharmacies. There were two types of concession. The first was based on a 'general right', which applied if the owner of the pharmacy was not a professional in this field; the second was based on a 'personal right', which meant that a pharmacy could only be founded by a person holding a Master of Science degree in pharmacy, or a person of Serbian nationality with a Doctor of Pharmacy degree, who had a record of good conduct, or was a foreigner who would receive Serbian citizenship within a year. Pharmacists with extensive relevant work experience had a distinct advantage.

The development and position of pharmacy in Serbia after 1867 following the liberation from Turkey was

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directly linked to the economic, social and political opportunities available in the later decades of the nineteenth and early decades of the twentieth centuries. Pharmaceutical education in Serbia during this period was heavily influenced by the first professionals in this field, who were educated abroad. One of the most influential of these was the pharmacist Velimir Karić.

This article examines the development of pharmacy in Serbia in the late nineteenth and early twentieth centuries by exploring the life and work of the pioneering pharmacist, Velimir Karić. Karić was the owner of the first pharmacy to be opened in the newly-liberated southern part of Serbia in 1882, and went on to be president of the Serbian Pharmaceutical Society. The article describes the development of pharmacy education, arrangements for opening new pharmacies, and initiatives to maintain drug supplies in Serbia, whilst highlighting Karić's contribution to the professional, social and political life of the country from the late nineteenth to the early twentieth centuries. This study makes use of a variety of historical methods including the documentary analysis of primary and secondary data sources.

Figure 1. *Photograph of Velimir Karić. (Source: Mihajlović D. The Development of Health Services in Vranje. (Note 4) 1968)*

Velimir Karić's training as a pharmacist in Serbia

Velimir Karić was born in Kragujevac on 15 October 1859 into the family of a clerk (Figure 1). He started his career as an apprentice pharmacist (a three-year pre-study internship) in 1875 in the first pharmacy in the municipality of Šabac.[6] The pharmacy was owned by the pharmacist Franz Ludwig who died in the same year; afterwards it was owned by Friedrich Ritzinger.[7] During the first half of 1876 the activities of the Serbian army and of the civil healthcare service were dominated by preparations for the Serbian-Turkish War.

In April 1876, the Ministry of Defence requested that the Health Department of the Ministry of Internal Affairs ('the Health Department') – as the national body directing all activities regarding health policy – provide it with all available statistical data on the state of Serbian pharmacies, as well as the number of graduate and non-graduate persons studying pharmacy, in order to organize mobilization in case of war, and ensure that citizens were provided with a sufficient number of pharmacies.

Accordingly, all the local administrations sent in their reports on the number of pharmacies, the names of the pharmacists, the length of their service, and the number and names of both their qualified assistants and unqualified practitioners such as apprentices. Information about their activities, and their capability at performing the role of pharmacist, also had to be sent.

Velimir Karić's name was enrolled for the first time in the District Prefecture Register of Šabac. This noted that a seventeen-year-old apprentice pharmacist named Velimir Karić, who originated from Kragujevac, was carrying out his internship of two years and eight months in one of its public pharmacies. It also suggested that he was someone who might be engaged as an assistant pharmacist, even though he had not at that stage passed the professional examination for assistants.[8]

In June 1876 Serbia declared war on the Ottoman Empire. This first Serbian-Turkish War lasted around six months, coming to an end at the beginning of 1877. From the reports sent by the District Prefectures to the Ministry of Defence in the second half of 1876, it is apparent that in Serbia during that time there existed 20 pharmacies, which were staffed by 23 masters of pharmacy as well as 7 pharmacy assistants, 14 pharmacy associates, and 2 laboratory attendants.[9]

As an apprentice pharmacist, Velimir Karić was among 42 Serbian pharmacists and other pharmacy staff who were noted in the Register as being involved in the Serbian-Turkish war.[10] In accordance with the provisions of the 'Ordinance for appointing a pharmacist as well as setting and operating pharmacies,' which specified the conditions for him to start his internship in a pharmacy in Šabac, he was required to submit his certificate of birth and the transcript of his grades that proved his successful completion of his studies, and also the grades confirming his good conduct. This reference was used for his further enrolment (referred to in the report of the District Prefecture to the Ministry of Defence) that provided evidence of his competence to be engaged as an assistant pharmacist, even if he had not completed his three years of education.[11]

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Pharmacy education in Serbia in the late nineteenth century

In Serbia, at the end of the nineteenth century, pharmacy was studied at a number of European universities, but prior to these studies, it was compulsory to practice pharmacy and take a practical examination, so-called 'tirocinium'. Thereafter, intending pharmacists went on to study for a further two years. Those who went to pre-college practice and were preparing for the tirocinium examination were called 'tironi' or pharmacy dispensers. The Serbian Pharmaceutical Society was responsible for pharmacy education in the country. After passing the 'tirocinium' examination, the candidate acquired the title of 'pharmacy assistant' or 'pharmacy associate'. The examinations were taken at the pharmacy in the district concerned, and the members of the examination board were the district physicist, state chemist and two community pharmacists.

Having received the 'tirocinium' diploma, candidates could either continue in pharmacy or go to university. After completing two-years of university studies, the student obtained the title of master of pharmacy. But even with a college diploma, it was necessary to work even longer in practice, usually for up to five years, in order to obtain a licence to work independently and to apply for a concession.

All pharmacists with the master of pharmacy or doctor of pharmacy title, who acquired their bachelor's degree and the right to work independently in a pharmacy, but who did not have a concession to open their own pharmacy, were called pharmacy associates. The students of the first year of study could work as support staff in pharmacies and practice within. They were called aspirants. Also, there were those from the final years of study who worked at a pharmacy without a diploma because they had not passed the final examinations. They were called dispensers. Apart from pharmacy associates, none of the above was allowed to work independently in a pharmacy without the supervision of a pharmacist mentor.[12] Following the end of the Serbian-Turkish Wars in 1878, graduate pharmacy students returned to Serbia from Vienna, Budapest, Prague, Graz and Zagreb Universities.

Many pharmacists insisted on moving their concessions (their official approval for opening or closing a public pharmacy) to the newly-liberated places, but the Ministry of Foreign Affairs did not allow this, because this action might impair drug supply in the places that had recently been liberated in Serbia. A Law on Health Institutions, and a Law on Health Care and Public Health Protection, were passed in 1879; both came into force in 1881, defining the nature of pharmacy practice in Serbia.[13] In the next year the first proposals to amend the Law on Health Care and Public Health Protection were made. They were adopted on 11 July 1884 and renewed in 1891, when the Serbian Kingdom was ruled by the governors of King Aleksandar Obrenović.[14]

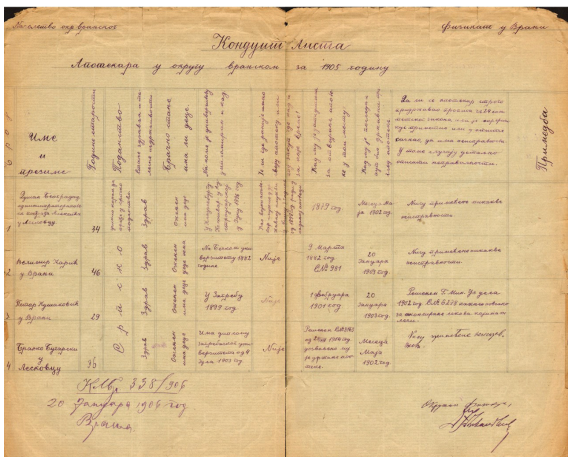

Figure 2. *Permit sheet of pharmacists in Vranje district. (Source: Historical Archive of Vranje '31 January', 1906)*

In 1882, Velimir Karić completed his pharmacy studies in Vienna, and he returned to Serbia to apply to open a new pharmacy in the newly-liberated town of Vranje in southern Serbia.[15] Examination of the approved list of apothecaries in the Vranje district since 1906, indicates that Karić's pharmacy received its permit to open on 9 May 1882 (Figure 2).[16]

Velimir Karić as owner of the first pharmacy in southern Serbia

According to the survey carried out by Krajnović and Arsić in 2014, the first pharmacy in Vranje actually started to operate before it was legally approved to do so, as it was technically already in the Commission's control in the hands of the state chemist, Ferdinand Šams (Franz Šams).[17] Velimir Karić managed his pharmacy in Vranje along the lines of the Viennese pharmacies where he had received his earlier training.

Pursuant to the provisions of the Law on Health Care and Public Health Protection, permission to open a new pharmacy was allowed in towns with less than 2,000 citizens. If the number exceeded 6,000 citizens a new pharmacy might be opened under certain circumstances. However, circumstances in the newly-liberated towns of Serbia were unfavorable, and Vranje had no pharmacy with a fully qualified pharmacist until 1882; the number of citizens in the territory of Vranje district was then 8,291.[18]

As pharmacists had a significant role in improving public health, their work was supervised in respect of both pharmaceutical services and their good conduct,

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pursuant to the Law on Health Care and Public Health Protection from 1879. This specified all aspects of the law relating to pharmacies and pharmacists.[19] Velimir Karić worked in Vranje until 1906,[20] and between the opening of the pharmacy in 1882 and 1906 – the period during which it was conducted by him – it was inspected four times by members of the Commission appointed by the Ministry of Internal Affairs through its Health Department.

According to directions made by the Ministry of Internal Affairs between 27 June and 2 July 1894, the appointed Commissioners carried out inspections of Serbian pharmacies until the end of the year. The Commissioners inspected Velimir Karić's pharmacy in Vranje on 9 December 1894, and made a report which was published in several Serbian Newspapers, including *Srpske novine*.[21]

Description of the pharmacy

The report stated that the pharmacy was located in the downtown part of the town in a very good location next to a house owned by the pharmacist. The pharmacy was marked out and had a night bell but, the Commissioners noted, there was no lantern on the pharmacy itself, although the house was located nearby only a few meters away. However, as the inspection was carried out according to the rigid rules of the Healthcare Code, the pharmacy owner was ordered to keep strictly to the law in future.

The pharmacy comprised five main elements: an office, a warehouse, a laboratory, an attic and a basement. In regard to its size and lightness, the office was managed in accordance with the requirements of the legal regulations. The drugs were kept on the shelves and in the drawers. Separate cupboards contained drugs with the highest potency. In the office were appropriate vessels for the preparation of watery and alcoholic solutions, syrups, ointments, extracts and powders, all of which were prepared by a pharmacist.

The most hazardous drugs – such as corrosive substances, arsenic, and atropine – were prepared in separate vessels. The Commissioners concluded that the office also included some substances which should not be there, such as 'Argentum nitricum' and 'Argentum nitricum cum Kalii nitrici', because they were sensitive to light. These preparations were found to be spoiled, and the Commissioners ordered that they be destroyed.

Although small, the warehouse of the pharmacy satisfied minimal functional requirements. Besides shelves, in the warehouse there was also a special cupboard for the storage of dangerous drugs and materials, that were kept in suitable containers. A wide range of essential utensils were kept in the laboratory, although this also was considered small. The equipment included distillation apparatus, an oil-squeezing press machine, a tincture press machine, and other utensils in conformity with the Health Code (book IV, volume II).

The pharmacy attic was described as spacious, and it contained cupboards with herbal drugs. The Commissioners noticed that it also contained cupboards with keys, which were used to store and preserve narcotic drugs, although they noted that there was no separate department within the pharmacy responsible for their preservation. They also noted that these cupboards were used to store only two narcotic drugs. Velimir Karić was advised to fill the cupboards with drugs, and to open up a suitable entrance from the pharmacy to the attic.

In the basement, the Commissioners noticed a few bottles without labels or written signatures, and also some cupboards that were too small to store acids in accordance with the regulations; instead, they were kept on open shelves away from the cupboards, in contravention of the regulations. The Commissioners required a new cupboard to be made, and also demanded that additional signatures be required in appropriate circumstances.

On completion of the inspection of the pharmacy premises, the Commissioners proceeded to check the drugs themselves. Qualitative examinations were carried out on the most frequently administered drugs, and also those used in the treatment of the most common diseases. Following these checks, a number of drugs were removed, either because of their inappropriate or ineffective content, or because they were well past their shelf-lives. The Commissioners insisted that all irregularities must be rectified.

The Commissioners also checked the protocols in use for the preservation of reagents intended for making drugs, for using vessels, and for analytical equipment. They ordered that the most important equipment for carrying out analyses must be provided. They also noted that the pharmacy had very good equipment for making soda. At the time, Velimir Karić was the only pharmacist operating in this pharmacy. He was found to be in possession of all required technical literature, as well as a book of recipes and a professional magazine.

Further control of the 66 Serbian pharmacies was carried out within a comprehensive supervision regime between 1901 and 1904.[22] A second audit of Karić's pharmacy was carried out in January 1903. According to the official record, it completely fulfilled the statutory requirements – as laid down in the regulations – as far as its equipment, stock and space was concerned. The Karić pharmacy was one of 27 Serbian pharmacies marked as being 'without irregularities'. Less serious

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irregularities in the remaining pharmacies were corrected, and confirmed through further audits by the Commissioners.

The district physicians also submitted reports on the work of local pharmacies, in lists of professional conduct submitted to the authorities. In the Conduct List of pharmacists from the Vranje district submitted on 20 January 1906 the district physician, Dr Đorđe Brzaković, made a number of comments about the activity of the Karić pharmacy, concluding that it had no irregularities.[23] The records also include details of the bills sent to the Health Department of the Ministry of Interior from the Vranje directorate, with one note stating 're-payment of tax paid by Velimir Karić, pharmacist'.[24]

Velimir Karić and a new pharmacy in Belgrade

At the end of the nineteenth century, there were 72 pharmacies operating in Serbia.[25] Besides the 72 pharmacist owners, there were 35 pharmacists with the Master of Pharmacy degree, and 54 assistant pharmacists. All the pharmacists and assistant pharmacists were Serbian citizens.[26] By the beginning of the twentieth century an increase in both the number of pharmacies and the populations in Serbian towns resulted in many problems in relation to concessions, which needed to be resolved. These came to a head in 1906, when the need to open a new – fifteenth – pharmacy in Belgrade emerged.

Many pharmacists from the interior wished to take the opportunity to move their pharmacies to Belgrade. This raised the question of whether it would be necessary to obtain the same rights for those pharmacies if they already had the concession in another place, or whether it was possible for them to lend or sell the concession in order to obtain the right to apply for the opening of the new pharmacy in Belgrade. Accordingly, the Serbian Pharmaceutical Society on 22 January 1906 addressed the Health Department with a request:

> We are asking for a solution for those who received a concession…[to open] a pharmacy in a certain place and they …[subsequently] sold it: if they still have the right to open a new pharmacy [elsewhere] due to the official announcement.[27]

The Health Department confirmed that pharmacists who had returned the concession for a pharmacy in one place had the right to open a new one in a new place. Ten candidates of Serbian origin applied to open the fifteenth pharmacy following the announcement issued in spring 1906. One of these was Velimir Karić, who applied to open a new pharmacy in Belgrade on 21 April 1906. The Directorate of Vranje confirmed that he could close his pharmacy in Vranje and apply to open a new one in Belgrade.[28] In due course the concession was awarded to Karić, who by then had been the longest qualified pharmacist, at 26 years, 7 mouths and 14 days.[29] The announcement applied to the Belgrade region of 'Savinac'.

In accordance with the regulations, Karić needed to open his pharmacy within a year, and to call the Commissioners of the Health Department in Belgrade to approve its opening following inspection.[30] But Karić encountered new difficulties, because he could not find an appropriate location for his pharmacy. Accordingly, he asked the Health Department to extend the geographical area for opening a new pharmacy, and this was approved.[31] However, close to the recently-extended area identified for this new pharmacy were the pharmacies of other pharmacists – his colleagues – who complained about the decision made in favour of Karić. However, this was later resolved in favour of Karić.[32]

According to research conducted by Arsić and Krajnović, Velimir Karić owned his pharmacy in Belgrade on 45 Makenzijeva Street until the end of 1926, when another pharmacist, Milan Živković, succeeded him.[33, 34] Karić had a brother Vladimir, who was a prominent geographer and a diplomat. After he died on 21 October in 1946 in Belgrade, he left all his properties to the Belgrade University fund for talented students. He was buried in New Cemetery in Belgrade.

Velimir Karić as president of the Serbian Pharmaceutical Society

In addition to the activities and achievements listed above, Velimir Karić was president of the Serbian Pharmaceutical Society ('the Society') from 1920 to 1924, a role he took on at the age of 60. He had been an active member of the Society for a number of years, being engaged in resolving numerous problems that the pharmaceutical profession encountered in that period. The Society had been founded in 1879.[35] In 1910, it launched a project to introduce a new law on healthcare practice management, based on a proposal to entirely restructure the pharmacy profession.[36]

It was proposed that, rather than all pharmacies being in state ownership, some should be available for private ownership, i.e. that it should be possible for individual pharmacists to open a new pharmacy when a need arose because of an increase in the number of citizens. The draft proposal was also supported by some unqualified druggists (i.e. owners of drugstores), because they wanted to change the status of their drugstores into privately owned pharmacies through the new system, while the young doctors who were active in the Serbian Medical Society wanted to abolish concessions for pharmacies altogether.

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The Serbian Pharmaceutical Society had many meetings in order to resolve this question, and eventually they decided to elect the delegates who would take part at a meeting of the Serbian Medical Society in August 1911.[37] One of these was Velimir Karić, who pleaded that the Serbian Pharmaceutical Society should maintain its support for the system based on concessions. Unfortunately, these disputes were not resolved, and the pharmacists did not reach consensus amongst themselves.

The resolution of further disputes was interrupted by first the Balkan Wars and then the First World War. The Society's other activities were carried out without problems until the outbreak of these wars. No activities were then carried out, because pharmacies operated under severely constrained circumstances with great difficulties; many of them were closed.

The period between 1912 and 1918 was very unfavorable for pharmacists in Serbia. The pressing need was to maintain the supply of drugs for the population. Following the departure of the allies in 1918 Serbia was left with an extreme shortage of drugs and a very difficult financial situation. Pharmacists found themselves with many competitors, who constantly attempted to turn pharmacies into free and unregulated drugstores.

After the end of the First World War, Velimir Karić continued to defend the system based on concessions, arguing that if the proposed system for the unregulated opening of pharmacies was supported, pharmacists would lose their public reputation, and in due course they would be seen as little more than clerks. Karić was anxious to emphasize the other professional aims that had led to the foundation of the Serbian Pharmaceutical Society in the first place.[38] The Society was engaged in an increasing number of activities, and a range of new professional tasks required the Society's administration to be extended. At the annual meeting of the Society held on 12 December 1920, a new administrative board of the Society was elected, with Velimir Karić as its president.[39]

Pharmacy in Serbia and the Chamber of Commerce

The new team at the Society initiated an intense programme of activities. They were engaged in founding a new Pharmacy Chamber, as well as in adopting drafts for the new healthcare law, the law on pharmacies and pharmacists' fees, and in opening a department for pharmaceutical studies at Belgrade University. As president of the Serbian Pharmaceutical Society, Velimir Karić was involved in the Board that in 1921 elaborated the draft of the healthcare law. He attempted to include the provisions based on concessions in the part of the healthcare law referring to pharmacists, but the project was defeated by the other Board members, mainly doctors.

Velimir Karić was also president of the Society when, in 1924, pharmacies were deemed to be retail shops, and came to be supervised by the Chamber of Commerce. This resulted from inconsistencies in the law, as authority to give approval for the opening of new pharmacies was given to the Chamber of Commerce, covering all types of business.

Pharmacists argued that the involvement of the Chamber of Commerce was illogical, because pharmacists received the concession to open a pharmacy based not only on competition, but also on the fact that they fulfilled substantial additional requirements laid down in the Law on Healthcare and Public Health Protection, and on the basis that they paid additional taxes stipulated by the tax laws.

Pharmacists considered that if they received a concession and their pharmacies were controlled before their opening, they had already gained credibility and had already been subjected to compliance with the specified regulations. This situation led to heated discussions within the Serbian Pharmaceutical Society about the need for the Society to found a separate Pharmacy Chamber, to manage the commercial aspects of pharmacy. In the opinion of its proponents, the problems would be solved by passing authority to issue permission to open a new pharmacy to the proposed Pharmacy Chamber from the Chamber of Commerce.

Accordingly, the Ministry of Health addressed an official letter, stating its final opinion on the matter. It supported the creation of a Pharmacy Chamber. It pointed out that pharmacies are health institutions which are supervised by the Ministry of Health. Thus, they could not be considered as simply commercial shops, and they should not therefore be supervised by the Chamber of Commerce. The Ministry of Health instructed all district authorities to stop all further controlling procedures aimed at the inspection of pharmacy operations; and on the basis of Constitutional Law, the Ministry empowered the Pharmacy Chamber to have authority across the entire Kingdom. All requests for new pharmacies already submitted to the Chamber of Commerce had to be forwarded to the new Pharmacy Chamber.[40]

Owing largely to the firm attitude of Velimir Karić, as president of the Serbian Pharmaceutical Society, the pharmacy profession in Serbia survived. The Society played a significant role in founding the Department of Pharmaceutical Studies at the University of Belgrade in 1921.[41] After many years of delay, universities in Belgrade, Zagreb and Ljubljana at the beginning of 1937 decided that the Faculty of Medicine in Belgrade

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should have two departments: medical and pharmaceutical. This initiative was implemented on 28 April 1939.[42]

Velimir Karić also contributed to the editorial activities of the professional journal *Glas Apotekarstva* ('The Voice of Pharmacy'). He resigned as president of the Society in December 1924. The Assembly rewarded him for his achievements and appointed him as an honorary president.[43]

Velimir Karić and drug supply in Serbia

The wars that Serbia carried out in 1912 and 1913 had a great impact on the position and state of the pharmacy profession in Serbia, and were particularly reflected in drug supply. Other impacts of the wars were that a substantial number of pharmacists died in them; at the same time many foreign drugstores had stopped their export of drugs to the country. There was no pharmaceutical industry in Serbia until the First World War. Certain pharmacies only produced some of their specialties. Drug supply in Serbia was dependent on imports from Austria and Germany.

The occupation of Serbia during the First World War had led the Serbian pharmaceutical service into an extremely difficult situation. Serbia was unable to obtain drug supplies during the occupation; what drugs they had in stock were stolen, and fresh drug supplies were prohibited. Serbian people were left to treat themselves with folk herbal drugs. The problem of obtaining drug supplies at that time was left to pharmacies, because the newly-founded Ministry of Internal Affairs was neither fully established nor able to find appropriate solutions to the problem. Illicit drug markets were normal and common practice. People who were not pharmacists traveled abroad to supply drugs. Pharmacists too found it necessary to obtain drugs in this way, but they were also responsible for the quality and safety of the drugs. Therefore, this way of obtaining drug supplies had to be stopped.

In the 1920s pharmacists found themselves in an extremely difficult situation as a result of war devastation; there were severe shortages in the resources essential for the normal functioning of their pharmacies, and for meeting the most urgent needs of the population in terms of drugs and healthcare materials. In the first days after the end of the First World War, the Ministry of Public Health – as a newly established government department within the Ministry of Internal Affairs – was unable to find a way of providing pharmacies with essential drugs and healthcare materials. The protests of individual pharmacy owners against the Ministry of Public Health – as well as the activities of pharmacy organizations – requiring urgent intervention in order to provide drugs and other equipment to pharmacies, were in vain.

The Ministry of Commerce and Industry, The Ministry of Food and Earth Restoration, and the Ministry of Finance, did everything they could to facilitate the transport of goods and materials. These institutions did their best to establish commercial and credit connections with contacts in the three allied states of France, England and America. A number of pharmacists attempted to restore the operation of their pharmacies by themselves, but their efforts remained largely unsuccessful due to the fact that:

1. In Serbia they often could not get affordable credit, whether because of the shortage of money or the extortionate rates charged by private capitalists, who gave the money;
2. Goods delivery from abroad was impossible, due to shortages in suitable means of transport, resulting in enormous difficulties and endless payments;
3. The delivery of goods was usually carried out by unqualified, unscrupulous tradesmen, who charged exorbitant prices for drugs. It therefore fell to the Ministry of Public Health to make the huge effort needed to make pharmacy credit available from state resources, and to facilitate the transport of both drugs and pharmaceutical materials from the allied countries.[44]

But the foundation of the Kingdom of Serbs, Croats and Slovenes on 1 December 1918, followed by the proclamation of the Kingdom of Yugoslavia, did eventually bring about remarkable transformations in Serbian pharmacy, as well as in other parts of the new state. These transformations resulted from immense economic, social and political changes, and were reflected in the organization, legislation and position of pharmacy in the country.

However, the legislation that Serbia passed in the twentieth century responded neither to pharmacists' professional requirements nor to the spirit of the time. The concession-based system remained in force until the end of the Second World War. The restrictions applying to increasing the number of pharmacies on Serbian soil depended on regulations requiring that opening a new pharmacy had to be directly dependent on the growth of the population in a particular area, regardless of the current circumstances and other needs.

This attitude made the position of pharmacists with a Master of Pharmacy degree very difficult, because they were prevented from receiving a concession to open a new pharmacy.[45] At the same time, graduate students with this degree could not get a job in an existing pharmacy, because to take on another pharmacist was very expensive; they could easily be replaced by an

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assistant pharmacist, who was able to operate in existing pharmacies after passing the licence examination; and they could not buy an existing pharmacy. So at that time, opening a retail drugstore was the only option available for pharmacists with the Master of Pharmacy degree.

The Shops Act 1910 and the opening of drugstores in Serbia

The Shops Act, which was passed on 9 April 1910, had provided an opportunity to open retail drugstores under certain circumstances. But it also created grounds for competitive confrontation between those pharmacists who were pharmacy owners and those who operated as pharmacist-druggists.[46] The conflict continued into the 1920s.

As soon as the Shops Act had been passed, the general Chamber of Commerce started to issue permits for the opening of drugstores, pursuant to Article 22 of the Act. According to this Article, pharmacies and drugstores were included because the Act's aims encompassed public security and health protection. Although rules made under the Act made it clear that they included decisions about when and where pharmacies and drugstores could be opened – and defined the criteria for opening drugstores in relation to the number of pharmacies – the Chamber of Commerce took no notice of these, but neither did they revoke the rules, leading to intense conflict and competition between pharmacies and drugstores.

On 14 August 1904 the Ministry of Internal Affairs stipulated special rules, based on the Law on Healthcare and Public Health Protection, which defined the number of opened drugstores in relation to the number of opened pharmacies. A drugstore could only be opened in a place where there were a greater number of pharmacies; where three pharmacies already existed, one drugstore could be opened. But the Chamber of Commerce still took no notice of the regulations nor revoked the order, and this was neither in the interests of the pharmacists nor of public health.

In accordance with the Shops Act, the Chamber of Commerce required the owners of both pharmacies and drugstores to report their activities and procedures to the Court. A great many complaints were sent to the Ministry of Public Health from unsatisfied doctors, until the problem was eventually resolved by passing the Pharmacy Chamber Provision on 21 February 1925. The Provision was issued in the Official Journal No. 39-IX, implying that only pharmacists could be members of the Pharmacy Chamber, and that responsibility for the opening of pharmacies and drugstores was removed from the Chamber of Commerce.[47]

The expansion of retail-scale drugstores in the 1920s

The emergence of drugstores was one of the key issues to be considered in evaluating the development of pharmacy in Serbia in this period. Serbia had neither a pharmaceutical industry, nor the institutions necessary to ensure adequate drug supply. Pharmacists began to join together and to search for the most suitable way of maintaining regular drug supply. Besides the small retail drugstores, there were also drugstores based on large-scale turnover – so-called large-scale drugstores – which were generally owned by foreign manufacturers and which also dealt in a wide range of healthcare materials.

Pharmacies and other healthcare institutions were supplied with drugs from both retail-scale and large-scale drugstores. Due to the existence of many retail-scale drugstores, and of specialized commercial shops dealing with herbal drugs, finished drugs, healthcare material, medical instruments – as well as with manufacturing and dispensing drugs on prescription – Serbian citizens were no longer aware of any shortages in drug supplies.

Following the end of the First World War many new large-scale drugstores were founded. Banks and foreign investors were very interested in founding companies for drug supply. At the same time Velimir Karić, as president of the Serbian Pharmaceutical Society, decided in Belgrade to import the most needed drugs, and to deliver them to pharmacies throughout Serbia.

Along with concerns about meeting the drug needs of the Serbian population, the confrontation between Serbian pharmacists and druggists about the location and number of drugstores continued. As druggists were not obliged to charge the official fees laid down for pharmacists when establishing the prices to be charged for selling drugs, they could sell them at a price lower than that charged in pharmacies. This situation created confrontations with pharmacists who were pharmacy owners. Druggists argued that in fact they were also pharmacists, having acquired Master of Pharmacy degrees, and that therefore they were professionally entitled to manufacture and sell drugs. But a few of these pharmacists were later prosecuted by the Ministry of Public Health for dispensing drugs on prescription, and for not respecting the rules on the opening and keeping of drugstores.

Given that – pursuant to the Law on Healthcare and Public Health Protection – the exclusive right for the manufacture and dispensing of prescription drugs was held by pharmacies, drugstores were strictly prohibited from dispensing such drugs. The Minister of State for Serbs, Croats and Slovenes received many complaints from doctors and pharmacists about the

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dispensing of prescription drugs by certain druggists, despite this being explicitly prohibited by law. In order to implement this prohibition, the authorities implemented extremely rigid audits of drugstores' work.[48]

There were eleven drugstores in Belgrade in 1922.[49] In 1923, there were already eighteen drugstores and twenty-three public pharmacies.[50] The number of retail-scale drugstores also increased in the interior. The reasons that induced pharmacists to open retail-scale drugstores after the war remained the same. Druggists joined together to defend their opinions and position. In 1924, they founded their own association, named 'the Association of Druggists of the Kingdom of the Serbs, Croats and Slovenes' (Udruženje drogerista Kraljevine Srba, Hrvata i Slovenaca).

The problem of sharing responsibilities and clarifying the relationship between drugstores and pharmacies continued, until it was finally resolved in the 1930s. Retail-scale drugstores remained in existence until 1928, when a competition for the opening of 26 new pharmacies was announced, in accordance with the legislative requirement that remained valid for the opening pharmacies taking account of the number of citizens.

For the 26 concessions for which the competition was announced, 17 concessions were awarded to druggists from Belgrade, and they thereby became pharmacy owners rather than drugstore owners, and the retail-scale drugstores went out of business.[51] The conflict, however, had an important impact on the passage of appropriate laws, and in promoting further improvements in the professional work of pharmacists.

Velimir Karić and the Pharmacy Buying Consortium

The drug supply problem remained, however, and with the aim of normalizing drug supply for the Serbian people, a wholesale company named Pharmacy Buying Consortium was founded by Velimir Karić, whilst president of the Serbian Pharmaceutical Society, together with pharmacists Radomir Stojić, Milan Mišković and Živojin Tasić. Given that they all had established reputations and extensive experience in business, the founders of the consortium succeeded in obtaining credit to build enough financial support. They organized a trip to Budapest for an urgent supply of medicines, that soon arrived in Belgrade on board the boat *Erzebet* at a critical moment.[52]

However, this delivery was not sufficient to meet the needs of both the pharmacies in Belgrade and of those in the interior. Mr Stojić therefore went to Vienna with a few of his colleagues, where he succeeded in obtaining and arranging transport for new deliveries of drug supplies for the whole of Serbia. Besides Vienna, members of the consortium went to Paris, Budapest, and a few places in Germany, where they bought a majority of the drugs required and sent them to Belgrade.

Given that only pharmacist Mišković had no pharmacy, the new buying consortium was called *Mišković and Company.* The consortium supplied the pharmacies in its own territory of Belgrade, as well as those in the interior. In 1920, the pharmaceutical wholesaling company called *Miskovic and Company* was registered in the Court of Commerce in Belgrade. The company operated under the title *Mišković and Company* until 1945, when it came under private ownership.

Due to its prompt delivery of goods, and timely and accurate payment arrangements, the consortium gained an excellent reputation abroad, as a result of which it was able to deal with the most prestigious companies. *Mišković and Company* was the agent for a number of large German, French and American pharmaceutical factories. The company also supported pharmacists with little money who hoped to open a pharmacy in a new place, even helping them with travel expenses. In time, *Mišković and Company* gained the reputation as Serbia's most significant company.

Drug quality control in Serbian drugstores continued to be implemented as a valuable procedure in the next decade in Serbia. According to the decree of the City of Belgrade, pursuant to the Act of the Ministry of Social Politics and Public Health dated 28 February 1935,[53] a three-member commission was established to control the drugstores on a regular basis. The Commissioners were the head of the Department of the Belgrade Directorate, the chief of the Pharmacy and Chemical Department of the Ministry, and the chief of the Department for Hygiene of the Belgrade Municipality.

Eight drugstores were covered by regular audits carried out between June and August 1935.[54] These included 'Braće Jugovića 'Izis'' (owned by Lavića Josića); the pharmaceutical wholesaler 'Embeskus' (owned by a pharmacist, Mr Subašić); the pharmaceutical wholesaler 'Mišković and Company' (owned by Smodlak Božidar); the 'Merkur' drugstore and 'Lamiko' (two shops owned by Svetolik Okanović, the heir owner of the drugstore 'Dvorske drogerije'); and the drugstores owned by the pharmacists Levi Solomon and Smodlak Božidar.

It is reported in the minutes of a completed audit undertaken on 15 July 1935 that the audit was attended by Velimir Karić and Milan Mišković, both of whom held the Master of Pharmacy degree. The Commission ascertained that the pharmaceutical wholesalers audited stocked only approved narcotics, drugs and medical specialities, and that all rooms and devices were in

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order, fulfilling all the statutory requirements and regulations.

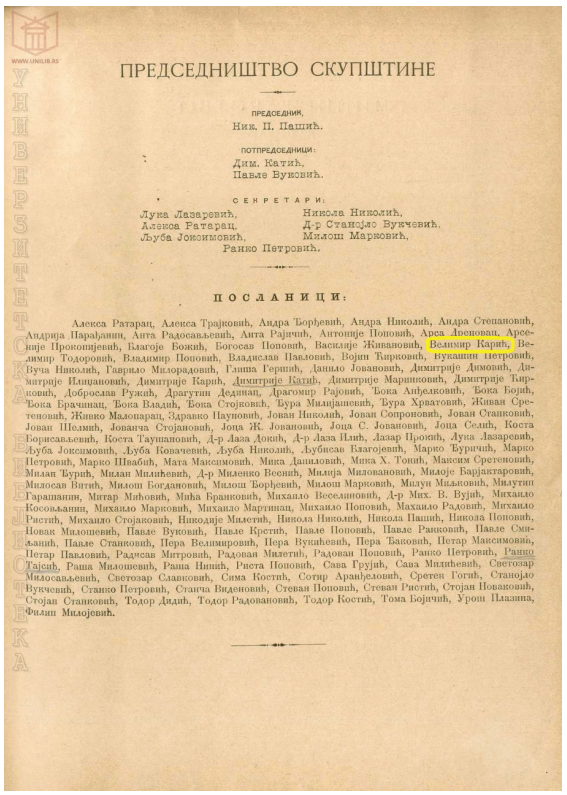

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Figure 3. *Notice confirming that Velimir Karić was elected as a city deputy in National Assembly of the Kingdom of Serbia. (Source: National Assembly, Official Gazette about National Assembly work. Belgrade: Državna štamparija Kraljevine Srbije, 1893:2)*

Velimir Karić as philanthropist

The contribution of Velimir Karić to the Serbian social community was also highly significant. As one of the leading intellectuals in Serbia at the time, Karić had many varied interests and professional involvements. His great ability, noble character, generosity and humanity made him a highly respected person amongst the citizens of Vranje, who elected him as a city deputy many times in the period 1893-1906 (Figure 3).[55] Amongst his many political engagements, he was the member of the parliamentary delegation that brought the King Petar Karadjordjevic to Serbia from Geneva in 1903,[56] who later became the last King of Serbia (1903-1918) and the first King of the Serbs, Croats and Slovenes (1918-1921).

In addition to his contribution to the pharmaceutical profession, Velimir Karić was a generous benefactor to numerous associations and individuals. For his achievements on the national level, he was awarded the Royal National Order of the White Eagle of the Fifth Class.[57] On the occasion of the Saint Sava day celebrations at the University of Belgrade, an annual award in the sum of 1600 Yugoslav dinars (about 30 U.S. dollars at that time) was established in the name of Velimir Karić.[58] On 28 January 1931, the first award from the Velimir Karić Fheavliy und was made to Miloš M. Petrović – a philosophy student at the University of Belgrade – for scientific achievements.[59]

Velimir Karić was a main board member for the organization established to build the monumental orthodox temple of Saint Sava in Belgrade.[60] He was the vice president of the Cultural and Human Society of Vračar,[61] which collected voluntary contributions for cultural and charitable purposes. He was a donor to the 'High School Society of War Orphans in Belgrade'.[62] He was a financial contributor to the Yugoslavian Society for the Study and Prevention of Cancer. And he was a donor of Christmas supplies for indigent war-disabled persons, and people suffering from tuberculosis.

Conclusion

This article has described the transition of pharmacy in Serbia during the late nineteenth and early twentieth centuries, with particular reference to the life and work of the pharmacist Velimir Karić. A key theme has been the impact of pharmacy education, examination and registration on practice. Different levels of education, particularly between those obtaining the Master of Science in pharmacy degree and those simply taking the licence examination, linked to regulations controlling the number of pharmacies that could be opened in a particular place, led inevitably to conflict and competition.

These issues pre-occupied the pharmaceutical organisations at the time, with the Serbian Pharmaceutical Society – representing pharmacists holding the Master of Science in pharmacy degree – keen to retain the concession-based system which was advantageous to its members. When a threat arose through the award of authority to give concessions being given to a Chamber of Commerce, the pharmacists were successful in persuading the government to create a separate Pharmacy Chamber and for this body to be given sole authority to award concessions.

Pharmacy in Serbia has also been heavily shaped by the wider political history of Serbia, especially the series of wars it was involved in during the late nineteenth and early twentieth centuries. This impacted especially on the supply of drugs and medical equipment, and led to initiatives by pharmacists to maintain such supplies. These included the creation of a Pharmacy Buying

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Consortium which applied to the whole of Serbia and later became a very successful commercial organization.

At the centre of all these developments was one man, the pharmacist Velimir Karić. He had been the owner of the first pharmacy in the newly liberated town of Vranje in southern Serbia in 1882; he had fought for the creation of a separate Pharmacy Chamber, and was the driving force behind the creation of the Pharmacy Buying Consortium. He served as president of the Serbian Pharmaceutical Society between 1920 and 1924; and he was also a generous philanthropist and benefactor.

From the evidence presented in this article it is thus clear that Velimir Karić left an outstanding legacy to the Serbian pharmaceutical profession, having had a very wide range of interests in the professional, political and social life of Serbia during his lifetime.

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Note

Some small portions of the results presented in this manuscript have previously been presented by the authors. See Arsić, J. and Krajnović, D. Pharmacy network expansion: on the trail of the advertisement for the opening of the fifteenth Belgrade pharmacy at the beginning of the twentieth century. Fourth International Congress of Pharmacists of Bosnia and Herzegovina, 10-13 October 2019. Proceedings book: 104-105.

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ARTICLE

Challenges and opportunities for western pharmacy in Colonial Hong Kong, 1945-1984

Patrick Chiu

Abstract

The period of resumed British colonial rule in Hong Kong from 1945 until 1984 – when the decision was taken to return sovereignty to China – presented both challenges and opportunities for pharmacy. The challenges included a rapidly expanding population, infectious diseases, a rise in drug addiction, and the impact of regional conflicts such as the Korean War. In response, the role of pharmacists became more important in controlling the supply of antibiotics, dangerous drugs and poisons. Changes were made to pharmaceutical legislation; a Pharmacy Board was created, becoming the Pharmacy and Poisons Board in 1969. A Pharmacopoeia Ordinance in 1958 resulted in the adoption of the *British Pharmacopoeia* in Hong Kong. This article illustrates how western pharmacy in Hong Kong adapted to the social, economic and political circumstances in which it found itself.

摘要 (繁體中文)

一九四五年八月二戰結束後,英國在香港恢復殖民統治直至香港未來的主權在兩國政府於一九八四年年底決定在1997年回歸中國的期間, 公立醫院提供的醫藥服務有著快速增長。

藥物立法的變化針對朝鮮戰爭 (1950 - 1954年) 以及吸毒成癮的新趨勢是為解決當時問題而採取必要的措施。然而, 1958年將"英國藥典"立為"國家藥典"的決定被視為維護大英帝國的長遠利益因為大多數在本地人還是首選中醫藥為治療方案。

處方醫生的繼續存在, 沒有把診症與藥劑服務的責任區分, 令到社區藥房仍然停留在香港在19世紀中葉成立時的實踐。

Introduction

After three years and eight months of occupation by the Imperial Japanese Army, Great Britain officially regained Hong Kong as a Crown Colony on 30 August 1945, at the end of the Second World War. This period had been one of the darkest in Hong Kong's history, with only 600,000 people surviving, or one-third of the original 1.8 million population in 1941. The British Military Administration was responsible for the resumption of governance in Colonial Hong Kong, until the civilian government restarted operations in May 1946.

The development of western pharmacy shifted gears soon after the end of the Second World War amid fresh waves of migrants – comprising entrepreneurs, investors, professionals, and workers from Shanghai and the Southern provinces, regions which were enduring difficult periods of civil war, regional conflict, and famine at the time. These migration patterns were seen from the mid-1940s until the 1970s, with resulting family reunions continuing from the 1980s until the 1990s.

The adoption of the *British Pharmacopoeia* as the national pharmacopeia was enacted in the Pharmacopoeia Ordinance of 1958 in Colonial Hong Kong. This was an example of efforts by the British government to consolidate its influence in local medical and pharmacy practice, despite Traditional Chinese Medicine still being the preferred method of treatment for a majority of local residents in the 1950s.

The weakness of low tax, laissez-faire economic models, and out-dated non-interventional policies (dating from the nineteenth century), once again exposed the need for a national healthcare service, especially in such a highly urbanised and affluent territory as Hong Kong.

As a result, community pharmacy development suffered, and it did not keep pace with the colony's burgeoning economic development of the 1950s. The continuing practice of dispensing by financially motivated private practice medical practitioners made this problem worse. These practices had exposed many inadequacies, including the indiscriminate issue of prescriptions for benzodiazepines and the dispensing of prescriptions by non-qualified clinic staff.

This article documents the challenges after the Second World War, and also explores the background to the development of western pharmacy in Colonial Hong Kong, from the latter-half of the 1940s to 1984 – when the Joint Declaration of the Government of the United Kingdom of Great Britain and Northern Ireland and the Government of the People's Republic of China on the Question of Hong Kong was signed.

Population growth, diseases and pandemics

The history of Hong Kong from 1945 to 1984 is one characterised by steady growth during the 'closed door' period of the Chinese Mainland. This growth was interrupted briefly by several regional conflicts, including the Korean War (1950-53), followed by the Vietnam War (1955-1975), and an over-spilling effect of the Cultural Revolution (1967-1976) in China. Hong Kong's population increased from 600,000 in 1945 to over 5.4 million in 1984 over a period of forty years, with three waves of immigration from the Mainland to Hong Kong (Table 1).[1]

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Table 1. *Hong Kong Population Increase, 1946-1980*

Mid-Year	Population '000	Estimated Migrants Increase in '000	Remarks
1946	1,168	500	Arrival of 500K migrants from September 1945 to mid-year 1946 and another 500K arrived in the second half of 1946.
1950	2,265	400	Civil war in China with 600K arrivals from 1947-1950 including 400K arrivals between1949-1950.
1960	2,981	100	Great famine started in 1959 and lasted until 1962.
1970	3,941	300	Cultural Revolution commenced in 1967.
1980	5,040	500	Cultural Revolution continued up to 1976 and there-after followed by Vietnamese "*boat people*" exodus of 1978-79.

The first and biggest wave of immigration occurred when one million people returned to Hong Kong within sixteen months after the Japanese surrender in August 1945. The population swelled to 1.6 million by the end of 1946. The second wave occurred at the end of the civil war in Mainland China in 1949, resulting in the fall of republicanism and the subsequent rise of communism. The population of Hong Kong further swelled from 1.9 million in 1949 to 2.3 million in 1950, an increase of 400,000 within two years.

The third period of immigration ran from 1972 to 1980. This period encompassed the 'Cultural Revolution' of 1967-1976 in the Mainland, and the exodus of the Vietnamese 'Boat People',[2] with 68,000 alone reaching Hong Kong as the first port of call in 1979. During this period, a total of 500,000 migrants arrived in Hong Kong, and the population jumped to 5.1 million in 1980.

To address possible adverse health consequences of such a rapid increase in population, vaccination programmes and improvements in hygiene and sanitary conditions – through infrastructure investment – were introduced, as well as the promotion of healthy living targeting particularly at housewives and school children (Figure 1).

Tuberculosis (TB) however continued to haunt Hong Kong throughout this period, and was attributed

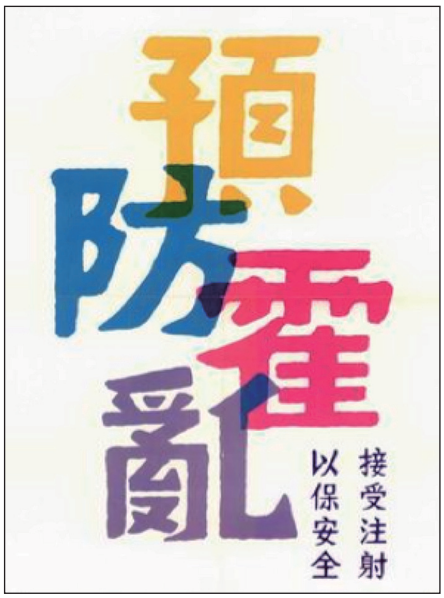

Figure 1. *Post Second World War poster of vaccination against cholera (Source: Government Record Service, Hong Kong)*

mainly to poor nutrition and overcrowded living conditions among the large migrant population from the southern provinces. In 1939, TB became a notifiable disease in Hong Kong, and in 1947, the first public service centre for TB was established at the Hartcourt Health Centre in Wanchai, followed by a few clinics across the colony. The highest death rate of TB recorded in Hong Kong – at 697.2 per 100,000 population – occurred in 1952.[3, 4]

Initially these centres provided limited facilities, such as the provision of vitamins, tinned food, milk powder, and rice. TB was the leading cause of death in the early 1950s, and would remain so until eventually being superseded by cancer in 1970. The average age of death was 25, but the illness was especially prevalent among young children, and many babies died as a result. However, the rate of tuberculosis in young children – especially those with meningitis – declined significantly soon after BCG vaccinations were introduced in 1952.

In 1950, specific treatment with anti-TB drugs was introduced in Hong Kong with the use of para-aminosalicylic acid. Active joint research was conducted between the Chest Service of the Medical and Health Services Department and the TB and Chest Unit of the Medical Research Council of the UK. Further drugs followed: streptomycin was introduced in 1951 and isoniazid in 1952.[8] Effective combination therapy then became readily available.

In the 1950s and 1960s, only about one quarter of patients completed their treatment, and the dangers of drug resistance and unsupervised treatment became

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Table 2. *The Five Leading Causes of Deaths 1950-1984*

Leading Causes of Death	1950 (no. of deaths)	1960 (no. of deaths)	1970 (no. of deaths)	1980 (no. of deaths)	1984 (no. of deaths)
1	Pneumonia (4,485)	Pneumonia (2,665)	Malignant neoplasms (3,964)	Malignant neoplasms (6,430)	Malignant neoplasms (7,369)
2	Dysentery and diarrhoea (2,514)	Malignant neoplasms (2,280)	Heart diseases (3,121)	Heart diseases (3,972)	Heart diseases (4,005)
3	Tuberculosis (Respiratory) (2,165)	Tuberculosis (1,907)	Pneumonia (1,985)	Cerebrovascular diseases (3,421)	Cerebrovascular diseases (3,220)
4	Congenital anomalies, immaturity etc. (1,262)	Heart Diseases (1,866)	Cerebrovascular diseases (1,806)	Pneumonia (2,277)	Pneumonia (1,883)
5	Tuberculosis (other forms) (1,098)	Cerebrovascular diseases (1,401)	Tuberculosis (1,436)	Tuberculosis (551)	Injuries and poisoning (1,593)

increasingly recognized. Supervised treatment – which was the forerunner of directly observed treatment (DOT) – was introduced on a trial basis in the 1960s. Since the 1970s, DOT has been delivered as part of the TB service. The six-month standard of a four-drug short course regimen with isoniazid, rifampicin, pyrazinamide, and streptomycin (or ethambutol), was introduced as early as 1979.

Over a period of forty years since the end of the Second World War, major disease patterns changed; infectious and parasitic diseases were the leading cause of death in the period between 1940 and 1960, along with infant and maternal mortality. This gradually changed, with evolution into cancers, heart, and cerebral vascular diseases were noted in the 1970s to 1980s with the exception of TB which persisted during the 1966 to 1976 period of the Chinese Cultural Revolution which was most probably due to the sudden influx of refugees across the mainland border (Table 2).

With Hong Kong being a major regional transport hub in Asia, and a highly dense population in a crowded territory of only 427 square miles (1,104 square kilometres), the transmission of infectious disease throughout Hong Kong – such as influenza – had on several occasions caused global pandemics throughout the period between 1945 and 1984. Drug treatment at the time was mainly palliative, since the approval of antiviral drugs such as Tamiflu® (oseltamivir) for marketing in Europe was only available in 2002.

The rise of drug addiction and the emergence of pharmaceutical control

Addiction to narcotics, especially by young people, is a complex economic, political and social issue. Harold Traver, in his book *Hong Kong Drug Business*, provided a summary of opium addiction:

> When Britain regained control of Hong Kong in August 1945, the British Military Administration issued a Proclamation (No. 13 of 1945) that suspended the Opium Ordinance of 1932 and classified opium as a dangerous drug subject to the Dangerous Drugs Ordinance of 1935. With repeal of the Opium Ordinance in 1946 (No. 2 of 1946), Hong Kong's long involvement in the sale of opium formally came to an end, though it took a couple of decades to root out opium smoking completely.[5]

The local trend in drug addiction changed from opium smoking to heroin (diamorphine) in the 1950s, and subsequently to methamphetamine in the 1990s. Cannabis and cocaine were more favoured by the expatriate community, and were not picked up as drugs of abuse by the local addicts, as heroin had been. Prevention of drug addiction posters were designed and displayed to target different segments of the community (Figures 2 and 3).

Barbiturates also became drugs of abuse when introduced as medicines in 1950s, but the supply was effectively controlled when barbitone, phenobarbitone and their salts were added to the schedule of Dangerous Drugs; dispensing was then required to be personally undertaken by qualified pharmacists.[6]

However, it was heroin that was the single drug of abuse that caused the widest extent of social problems amongst its most prevalent users – the young, male and under-employed social class. Methadone replacement therapy was introduced by the colonial Government in

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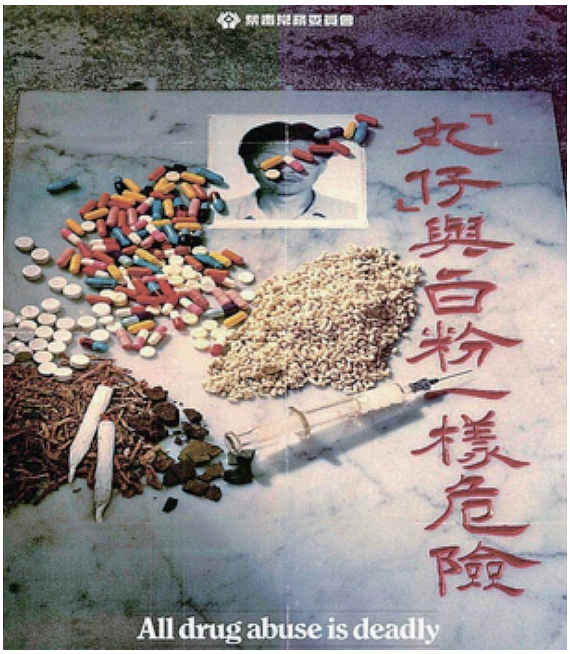

Figure 2. *'Pills and Heroin are Equally Deadly' poster (Source: Narcotics Division, Security Branch, Hong Kong)*

1972, and remains the gold standard in heroin replacement therapy today.[7]

Heroin use superseded opium use in the 1970s, as addicts found it much easier to administer, transport and carry, and financially it was more profitable for the drug dealers. Two studies conducted between 1962 and 1972 by Lau and Yap, and in 1972 by SARDA, showed that the number of current and initial opium users had declined by more than 30 per cent, while the number of current heroin users had increased by a similar amount (Table 3).[8]

A wide-ranging and multi-agency approach to drug treatment and rehabilitation services funded by the government was implemented. This included a compulsory approach for prison inmates, of whom 90 per cent had drug abuse history in the 1950s; this evolved into residential drug treatment for ordinary drug addicts in hospitals in the 1960s, followed by an out-patient approach in the 1970s which proved to be the most effective.

Methadone was used for three weeks for a detoxification programme, preceding a daily dose for the next six months with counselling (an integral component of the treatment regimen). A registered addict paid only a token fee of Hong Kong one dollar (ten pence) for each daily dose.

Other providers such as religious organisations and private counselling centres also provided drug treatment to addicts. Moreover, 1975 was the peak year of methadone out-patient treatment, when there was a global shortage of heroin and an average of 9,400 addicts waited for their daily dose at only twenty-five clinics in the colony.

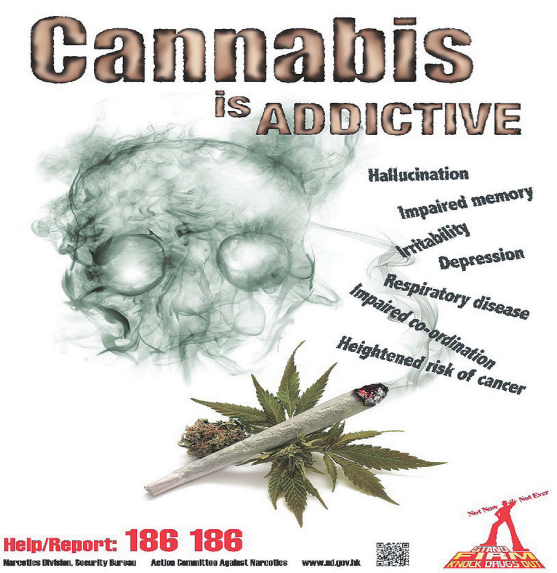

Figure 3. *'Cannabis is Addictive' poster (Source: Narcotics Division, Security Branch, Hong Kong)*

Drug addiction and the role of pharmacists

Following the end of the Second World War, the role of pharmacists became increasingly important in the control of sales of antibiotics, dangerous drugs, and poisons or prescription drugs, which reflected the state of diseas-

Table 3. *Change of Preference of Drug Addiction, 1962-1972*

Year	Addicts				
	Type	Opium Only	Opium Initially and Heroin Subsequently	Heroin Only	Total
1962-63 (Lau and Yap 1967)	Number	128	501	339	968
	% of total	13.2%	51.8%	35%	100%
1972 (SARDA 1972)	Number	87	0	525	782
	% of total	11.1%	25.7%	67.1%	100%

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es such as tuberculosis, drug addiction and also the shift in relative importance of particular diseases such as cardiovascular diseases in causing death. This led to subsequent legislations to regulate the sales, supply, distribution and manufacture of pharmaceutical products.

While the control of dangerous and psychotropic drugs was highly commendable – with a stringent penalty system operating for pharmacy owners and pharmacists in retail practice – a major loophole existed. When the pharmacists were off duty, and since most pharmacies generally remained open late, unscrupulous pharmacy owners (or shop assistants who were shopkeepers and not registered pharmacists) could supply these controlled drugs to patients without requiring prescriptions.

The late 1940s and early 1950s were characterised by immense regulatory control on the sale and use of antibiotics, mainly penicillin and streptomycin, which were in high demand. This was particularly the case during the second and final Nationalist and Communist civil war in the Mainland (1946-1949) and the Korean War (1950-1954).

The sale of such antibiotics was restricted for political and economic reasons. Firstly, such novel drugs to treat infectious diseases were extremely costly, and were not affordable by the working population. In October 1947, a Streptomycin Committee was appointed, with the government's Senior Medical Officer as its chairman, together with eight members representing the University of Hong Kong and the government.[9] In 1948, Chloramphenicol and Aureomycin were taken under the administration of the Streptomycin Committee, which controlled the treatment of cases receiving these antibiotics in Government institutions.

Secondly, a great demand for antibiotics to treat wounded soldiers at the war fronts in Korea made supply a nightmare, as a trade embargo for re-exports from Hong Kong to China was in place. Prices of penicillin and other antibiotics went up dramatically in the local market, and the colonial government stepped up the inspection of authorised sellers of antibiotics (i.e. pharmacies) to identify any sales taking place without prescriptions. Thomas Mahon, the then chief pharmacist, reported that:

> In January 1951 speculation in antibiotics became very prevalent with the result that it became virtually impossible for doctors and hospitals to obtain their requirements at reasonable prices. Emergency regulations were promptly introduced and price control was established where necessary. These measures proved effective.[10]

In November 1950, the administration of the Dangerous Drugs Ordinance was transferred from the Director of Commerce and Industry to the Director of Medical and Health Services. This move represented a new approach for drug addicts, especially those on heroin, where they were given serious treatment instead of imprisonment.

In 1948, preliminary work had been carried out on the formation of a Pharmacy Board which would control the training and registration of pharmacists in the colony. The Pharmacy Board was formally inaugurated at its first meeting on 12 February 1951. It consisted of:

- the Director of Medical and Health Services as chairman;
- the Professor of Chemistry at the University of Hong Kong;
- the Government Chemist as an ex-officio member;
- the Government Chief Pharmacist as ex-officio member;
- a Government Medical Officer;
- a legal adviser;
- three registered pharmacists appointed by the Governor as members.[11]

By 1958, the work of the Pharmacy Board had grown, with a major part of its workload being the introduction of subsidiary legislation for the control of habit-forming drugs, particularly certain tranquillisers. Attention was also given to the amendment of the Undesirable Advertisements Ordinance for the better control of the advertising of patent medicines purporting to provide relief or cure of insomnia.[12]

The Pharmacy Board eventually changed its name to the Pharmacy and Poisons Board in 1969. The membership of the Board expanded to eleven, with the position of professor of chemistry replaced by that of professor of pharmacology, and the addition of two private practice medical practitioners, with one representing the Hong Kong Chinese Medical Association and the other representing the Hong Kong Branch of the British Medical Association.[13]

The Pharmacopoeia Ordinance

The Pharmacopoeia Ordinance was passed in 1958 in response to the completion of the two-volume, first edition of *International Pharmacopoeia* by the World Health Organization (WHO) in 1955. Dr D.J.M. Mackenzie, Chairman of the Hong Kong Medical Council, approved the adoption of the *British Pharmacopoeia* as per Section 2 of the Pharmacopoeia Ordinance 1958 on 9 September 1958 (Figure 4). This was finally approved by Alan Lennox Boyd, the then Secretary of State for the Colonies, on 29 September 1958. The Director of Medical and Health Services articulated the

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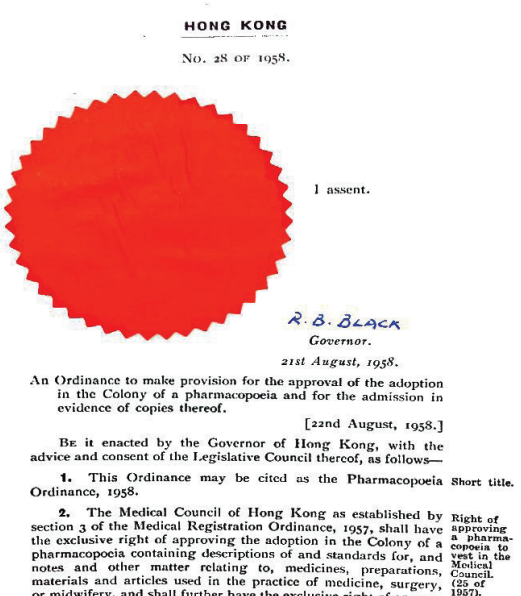
reasons for this development in his 1958 annual report of the legislation:

> The Pharmacopoeia Ordinance was enacted to enable the Medical Council (in Hong Kong) to approve the adoption in the Colony of a pharmacopoeia and thus, by giving official recognition to the standards therein specified, to remove uncertainty as to what are the proper ingredients and proportions of drugs bought and sold. This Ordinance further provides for the publication in the *Gazette* of the notification and adoption of a pharmacopoeia which can then be admitted in evidence in the Courts.[14]

The inclusion of the *British Pharmacopoeia* as the only national pharmacopeia ignored the fact that Traditional Chinese Medicine was still preferred by a large segment of the local Chinese population. This disregard has been commented on by Anderson:

> It has illustrated the [fact that the] function of the *British Pharmacopeia* in the early part of the twentieth century went far beyond specifying standards and rationalizing formulas. It played a part in regulating trade in drugs and medicines, by promoting western medicines at the same time as suppressing the use of indigenous medical education and practice.
>
> The issues encountered in India were repeated in many other provinces and settlements across the empire, with diverse climates, cultures, and religions. For imperial powers such as Britain, pharmacopoeias became instruments of imperialism.[15]



HONG KONG

No. 28 OF 1958.

I assent.

R. B. BLACK
Governor.

21st August, 1958.

An Ordinance to make provision for the approval of the adoption in the Colony of a pharmacopoeia and for the admission in evidence of copies thereof.

[22nd August, 1958.]

BE it enacted by the Governor of Hong Kong, with the advice and consent of the Legislative Council thereof, as follows—

1. This Ordinance may be cited as the Pharmacopoeia Ordinance, 1958. Short title.

2. The Medical Council of Hong Kong as established by section 3 of the Medical Registration Ordinance, 1957, shall have the exclusive right of approving the adoption in the Colony of a pharmacopoeia containing descriptions of and standards for, and notes and other matter relating to, medicines, preparations, materials and articles used in the practice of medicine, surgery, or midwifery, and shall further have the exclusive right of approving the adoption of any amendments thereto. Right of approving a pharmacopoeia to vest in the Medical Council. (25 of 1957).

Figure 4. *The Pharmacopoeia Ordinance 1958 (Source: Government Record Service, Hong Kong)*

In 1959, proposals for the amendment and re-enactment of the Pharmacy and Poisons Ordinance was completed and submitted to the colonial government for approval to prepare a draft bill. These included restrictions on the employment of part-time pharmacists, and simplification of the control of antibiotics, together with other suggestions intended to make the Ordinance more easily understood by the lay public.[16]

The part on employment of full-time pharmacists was rejected by the Hong Kong Medicine Dealers' Guild (a pharmacy owner's guild) for cost reasons,[16] which delayed the amendment to restrict the employment of part-time pharmacists by ten years, with the final enactment being the revised Pharmacy and Poisons Ordinance of 1969. Prior to that, some pharmacists 'leased' their registration certificates to several pharmacies at the same time to make up for a full-time salary.

In 1960, the main items of business considered by the Pharmacy and Poisons Board were agricultural poisons and the use of scheduled poisons – as well as heavy metals found in some of the raw herbs used in traditional Chinese herbal medicines.[17]

In 1975, important changes were recommended in the sale, supply and distribution of poisons, after consultation with the Pharmaceutical Society of Hong Kong. A motion was proposed by Dr Gerald Hugh Chao, the then Director of Medical and Health Services, at the meeting of the Legislative Council on 16 July 1975, to pass the Poisons List Regulations 1975 and also the Pharmacy and Poisons Regulations 1975. He explained the rationale of changes as follows:

> Their purpose is to enable more effective control to be exercised over the sale and manufacture of all pharmaceutical products in Hong Kong, and they include certain new provisions to this end. I emphasize at the outset that the Board's overriding concern has been to make adequate provision for the protection of the public as a whole. Included in the new provisions is a requirement for all pharmaceutical products, whether they include poisons or not, imported into or manufactured in Hong Kong, to be registered before they can be offered for sale.[18]

After much deliberations over the next two years, the laws eventually became effective in July 1978. The classification of medicines agreed is summarised in Table 4.

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Table 4. Classification of Medicines, 1978

Antibiotics/Poisons	*Class*	*Example*	*Prescription*	*Pharmacy*
Antibiotics	Aminoglycosides Penicillins Cephalosporins Tertacyclines	Stretomycin Ampicillin Cephalexin Chlortetracycline	✓	✓
Dangerous Drug	Narcotics	Cocaine, Diacetylmorphine, Morphine, Phentermine	✓	✓
Part 1 Schedule 3	Corticosteroids, Statins	Prednisone Lovastatin	✓	✓
Part 1 Schedule 1	Codeine cough syrup	(>0.1% Codeine)	×	✓
Part 1	Codeine cough syrup	(<0.1% Codeine)	×	✓
Part 2	Antihistamine Oral contraceptives	Chlorpheniramine (containing < 50 mcg oestrogen, < 5mg progesterone)	×	×
Non Poison	Cough and cold, Antacids etc.	Paracetamol Cimetidine	×	×

The changing political climate in London

Although Great Britain was not a supporter of the communist movement in China, the United Kingdom was one of the first countries to recognise Mao Zedong's government of the People's Republic of China in January 1950. In the interest of trade and retaining Hong Kong as a Crown Colony, negotiations were maintained and relationships were amicable. However, the political climate in London changed in the mid-1970s.

With growing recognition of the realities of handing over Hong Kong back to China in 1997, a series of initiatives driven by Downing Street led to increasing investment in higher education, infrastructure, hospital services, and other social welfare programmes, with the aim of raising and differentiating the identity of the Hong Kong people from their Mainland counterparts.

Ray Yap and Dai-Luk Lu, in their paper, described the dynamics of social reform under Murray MacLehose, who was the twenty-fifth Governor of Hong Kong between 1971 and 1982:

> The economic success of Hong Kong created some ripples in the political waters of the metropolis. As early as January 1967, a question was raised in the House of Commons on workers' conditions in Hong Kong as documented in the recently released archives of the Foreign and Commonwealth Office available at the National Archives.
>
> When more questions were raised in the Parliament – twice in April 1975 – the situation in Hong Kong, whose poor social welfare and inadequate labour protection were seen as factors contributing to Hong Kong manufacturers underselling British producers, became a matter of political concern to the British government. Political pressures were further consolidated by the publication of a Fabian pamphlet entitled "Hong Kong – Britain's Responsibility" in early 1976.

The British government's rising concern over Hong Kong's development also had another important strategic dimension: the future of Hong Kong. For London, one of the major lessons learned from the 1967 riots was that British rule in Hong Kong beyond 1997 was simply untenable. The revolutionary fervour unleashed by Maoist radicalism may have subsided by the early 1970s, but the incompatibility between hu-

Figure 5. *Deng Xiaoping and Margaret Thatcher during Sino-British negotiations on the future of Hong Kong in 1984 in Beijing (Source: Government Record Service, Hong Kong)*

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miliation inherent in the alien rule of Hong Kong and Chinese nationalism remained intact.[19]

Preparation for the transition of Colonial Hong Kong commenced at the same time when the 'Reform and Opening Up Policy' led by Deng Xiaoping, China's paramount leader at the time, was launched in 1978 in the Mainland.[20] The 1983 financial crisis arose in Hong Kong during the Sino-British negotiations on the future of Hong Kong, which resulted in a loss of confidence amongst investors, and subsequently led to the depreciation of the local currency by 50 per cent within a six-month period (Figure 5).

Conclusion

Rapid population growth was both an opportunity and a challenge in the development of western pharmacy during the forty-year period following the end of the Second World War. Pharmaceutical services in the public hospital sector saw rapid development in line with British hospital pharmacy practice in both routine and extemporaneous dispensing, and sterile and non-sterile manufacturing with the exception of clinical pharmacy which was not in existence, and in-house quality control which was out-sourced to the Government Laboratory for quantitative and qualitative analysis.

Although the results by the end of the forty-year period were largely positive, there were nevertheless setbacks in the process. It should also be clear to most readers that major reforms had yet to be made to bring the standard of western pharmacy in Hong Kong on a par with that in the community and industrial pharmacy sectors of other developed economies.

With the expected change of sovereignty of Hong Kong in 1997, anxiety and nervousness in the Colony began to surface in the early 1980s, and reached boiling point with the occurrence of the 1989 Tiananmen Square incident. The years 1985 to 1997 represent an historic transitional period in Hong Kong, as much for pharmacy as for other aspects of life in the colony. Developments during the period from 1945 and 1984 set the scene for what was to follow.

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20. The 'Reform and Opening Up Policy' initiated in 1978 turned China from an inefficient commune style planning economy to a vibrant market economy, resulting in poverty reduction of 1 billion out of 1.3 billion people in 36 years by 2014.

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ARTICLE

Controlling the quality of tablets: from their invention to the dissolution test

Axel Helmstädter

Abstract

The dosage form of tablets was invented by the British artist William Brockedon (1787-1854). He intended to produce dosage forms containing a minimum of excipients. Without any experimental proof, it was assumed that 'compressed pills' would disintegrate rapidly. First investigations into the disintegration of tablets were done by Silas Burroughs (1846-1895), co-founder of the Burroughs, Wellcome company. He and many successors revealed that tablet disintegration was – contrary to the initial assumption – a critical step for therapeutic success. However, various pharmacopoeial test methods developed slowly from 1907 onwards and remained rather primitive, until the *United States Pharmacopoeia XIV* in 1950 presented the first detailed test procedure. In the early 1960s, the introduction of physico-chemical knowledge, dating back to 1897, into pharmaceutical sciences led to dissolution testing as a central tool in modern biopharmaceutical considerations.

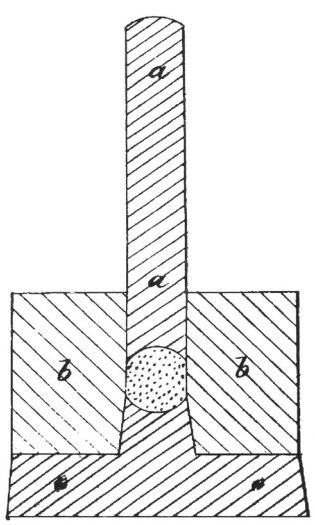

Figure 1. *Schematic drawing of the Brockedon press (Source: British Patent Office, 1844)]*

The Brockedon patent

In December 1843, the British artist and inventor William Brockedon (1787-1854) submitted a patent specification called "Shaping Pills, Lozenges, and Black Lead by Pressure in Dies". The patent, which was granted in June 1844, described the first, but rather simple, tablet press comprising a base with a central raised pillar in a metal collar, and a punch for the compaction of powders to one single tablet by manual hammer blow (Figure 1).[1] Brockedon however was not a pharmacist, and was primarily interested in recycling the lead dust from the debris released from the lead pencils he regularly used during his main business as a graphic artist.

Besides this, he developed the idea of compressing medicinal substances like potassium chlorate and sodium bicarbonate. The resulting 'pills' – in contrast to traditionally manufactured ones – did not contain any additional substances (excipients) like gum or other adhesive material. They were therefore considered extremely pure. At first glance, it seems strange that what is now regarded as the invention of the tablet – a new dosage form – was still called a '(compressed) pill'. However, even in the first decades after Brockedon's patent, the invention was simply regarded as a new production method of traditionally used oral dosage forms like pills, pastilles and lozenges.

In the second half of the nineteenth century, however, the 'compressed powders' gained increasing popularity as they were an easy-to-use dosage form. As they needed no liquid for production, they were much more stable than traditionally formed pills; they could easily be stored and transported, an advantage primarily attractive for their use in military pharmacy.[2] In contrast to manufacturing traditional pills and lozenges, powder compression made industrial production possible, and from the 1870s onwards a variety of tablet machines with continuously rising output were developed.[3]

The development was considerably triggered by the Burroughs, Wellcome company, founded in 1879 by Silas Burroughs (1846-1895) and Henry Solomon Wellcome (1853-1936). Burroughs had gained experience in pharmaceutical trading in the United States before entering the Philadelphia College of Pharmacy, where he graduated in 1877. Initially working as an agent for the American Wyeth company in Britain, he founded a local business together with Wellcome, and they introduced the tremendously successful trade mark *Tabloids*, registered in 1883. Two years before, Burroughs had travelled all over the world in order to promote and sell the company's products, which can be demonstrated by assessment of his extensive correspondence.[4]

Early considerations

While a variety of considerations had been made about manufacturing techniques of pills, including their gold and silver coating, nobody had considered either their disintegration in the gastrointestinal tract, or the liberation of drugs from the dosage form. In 1884, for example, pharmacist Hermann Hager (1816-1897) – a

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leading German author – devoted 40 pages of his influential book on pharmaceutical technology to the preparation of pills, but only mentioned dissolution problems in a few sentences. He only noted that pills stored for a long time could harden, such that physicians complained about the unchanged excretion of pills in the faeces. This could be avoided by the addition of a small amount of glycerin.[5]

Some years later, in the following edition of his work, Hager pointed out the importance of manufacturing pills that were capable of disintegrating and dissolving in the gastrointestinal tract, and again he recommended the addition of a small amount of glycerin, or small amounts of marshmallow root and tragacanth to avoid early hardening, but he did not recommend any test procedure.[6] This may not be surprising, as pharmacopoeias at that time primarily gave details of prescription formulas and production methods; analytical procedures for quality control were absent or only mentioned incidentally until the early twentieth century.

Even in 1920, Grönberg regarded the dissolution behaviour of pills in the gastrointestinal tract as an unsolved problem, and complained about a lack of published knowledge about this. He then reported on some disintegration experiments that he carried out himself with pills in artificial gastric juice, and found many of them were undissolved. He also observed reduced disintegration after storage.[7]

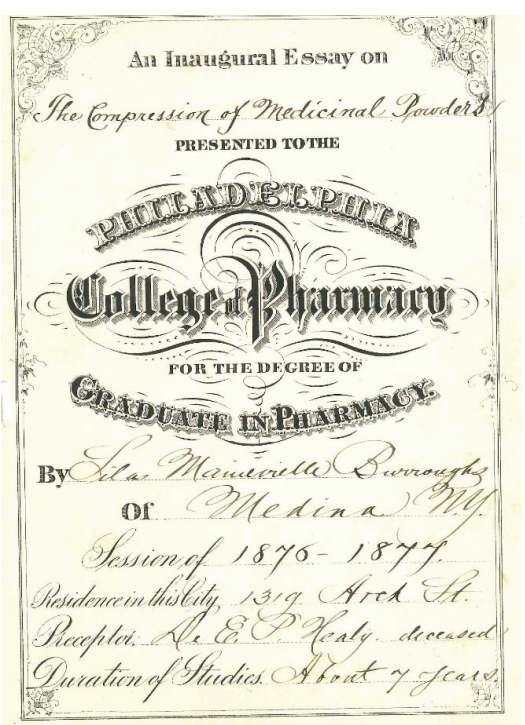
An Inaugural Essay on
The Compression of Medicinal Powders
PRESENTED TO THE
PHILADELPHIA
College of Pharmacy
FOR THE DEGREE OF
GRADUATE IN PHARMACY
By Silas Marinerella Burroughs
Of Medina NY.
Session of 1876-1877.
Residence in this City, 1319 Arch St.
Preceptor, Dr. E. P. Healy. deceased
Duration of Studies, About 4 years.

Figure 2. *Front cover of Silas Burrough's thesis (Source: Philadelphia College of Pharmacy, 1877)*

Burroughs' thesis

Silas Burroughs began important pioneering work in this field in 1877, devoting his thesis ('inaugural essay') at the Philadelphia College of Pharmacy to the 'Compression of Medicinal Powders'[8] and in particular to their disintegration properties (Figure 2). This was an entirely new approach to the evaluation of oral dosage forms which, unfortunately, exerted little impact on the development of pharmaceutical technology, as it remained unpublished.[9]

In the introduction to his thesis, Burroughs disagreed with the term 'compressed pills', although he had chosen it himself, probably due to its widespread use. Criticism concerned the fact that the term

> may imply their preparation from a pilular mass, in which an excipient has been employed, whereas, if properly prepared they are merely dry powders, compressed without addition whatever, except in cases where an increase of bulk is demanded, as in the case of powerful alkaloids […] where the dose is very small.[10]

Excipient-free production from dry powder was the reason why it was commonly assumed that these preparations always disintegrated rapidly, in contrast to traditionally prepared pills: 'It will be seen that since no water or other constituent is used, said tablets must dissolve readily in the stomach.'[11] As disadvantages, Burroughs mentioned high prices and low robustness: 'Another considerable objection to their use was the liability to break or fall in pieces upon slight exposure to the atmosphere or by rough handling or age.'[12] The tablets should therefore be compressed with appropriate pressure, protected from moisture and stored in boxes together with cotton.

Burroughs then reported on his own experiments, done 'with the view of ascertaining the solubility and diffusibility of these Compressed Powders'.[13] In his experiments, he determined dissolution or disintegration times of mostly quinine-containing, conventionally manufactured, partly coated, pills and 'compressed powders'. Interestingly, he tried to simulate gastrointestinal conditions right from the beginning, using water at body temperature (95-100 °F) with and without the addition of a certain amount of acid. He also suggested that disintegration experiments should better have been done in motion to simulate the physiological situation even closer.

The results clearly show that compressed dosage forms disintegrated in a timeframe between 3 and 20 minutes – thus much more rapidly than conventional pills needing between 30 and 70 minutes. In some

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cases, Burroughs gave two results, one for 'dissolved', one for 'disintegrated', showing that he already suspected the difference between these processes. Products prepared with glycerin as the only excipient were found to be superior to all others.

Burroughs suggested that 'compressed pills' disintegrated more quickly than traditional ones because 'the pores being open, give prompt admission to the solvent used'.[14] He admitted that medicines administered in solution or as loose powders would be the most preferable ones, but were in several cases not acceptable by the patient due to bad taste. Properly prepared compressed preparations, i.e. those without moisture or excipient, could easily and almost tastelessly be swallowed.[15] Somewhat surprisingly, the thesis ends with the conclusion that besides all the advantages of tablets over pills mentioned up to this point, they should also be able to constitute 'a protection against Homeopathic practice'.[16]

Varying quality of tablets

From the 1880s onwards, it became clearer that the disintegration properties of compressed tablets were not optimal in all cases. More and more reports about the unsatisfactory behaviour of tablets and unacceptable experimental results were discussed in the pharmaceutical literature. Schneider, for example, found a wide range of disintegration and dissolution times of preparations. Most tablets disintegrated within a few minutes; however, those containing salicylic acid remained unaffected for a few days.[17] Physicians complained about the unchanged passage of antipyrine tablets through the gastrointestinal tract.[18]

This provoked some awareness of the problem and was the starting point of a vivid discussion in the literature of the following decades. It is clear that at this time a learning process about the proper constitution of a tablet had started. It became clear that, on one hand, the products had to be sufficiently hard to be safely stored and transported; and on the other hand they had to disintegrate or even dissolve in gastrointestinal fluid sufficiently rapidly.

This antagonism was addressed by Eugen Dieterich (1840-1904), one of the most influential protagonists of pharmaceutical technology in Germany. As early as 1890, he gave tablet manufacturing specifications for the most commonly prescribed substances.[19] However, disintegration properties remained a central problem of pharmaceutical technology. In 1901, Carl Svante Hallberg (1856-1910), Professor at the Chicago College of Pharmacy, extensively discussed properties of several types of 'dry medication'.[20] He pointed out that water-insoluble active agents could obviously not be administered in solution, and must therefore be incorporated into solid dosage forms. However, he clearly foresaw what we call biopharmaceutical problems: 'Since they must be absorbed through solution, and must usually also be decomposed […] the *especial forms* of these solids should be designed with particular reference to secure the most prompt and active effect'.[21]

Early test procedures

Hallberg tested 'compressed tablets', pills and 'encapsulated powders' in 'gastric liquid' containing pepsin and hydrochloric acid, and in 'intestinal liquid' containing 'inspissated oxgall', pancreatin and sodium bicarbonate. The procedure was described as follows:

> The medicinal forms […] were put in long, narrow test tubes, with 25cc [cubic centimetre or ml] of the respective liquids, and maintained at a temperature of 37°C, for a period of four hours. The test tubes were gently shaken to dislodge undissolved matter, and then slowly moved every few minutes to secure an approximation to the peristaltic movement.[22]

He found different disintegration and solution rates, and concluded:

> The prominent fact is disclosed that the compressed tablet form is much inferior in the rate of disintegration to the pill or encapsulated powder. […] in the majority of the tablets […] the residue was the tablet form, practically intact, simply showing frayed edges.[23]

He then refuted the propaganda about tablets, and appealed to pharmacists' professional honour to prepare dosage forms selected from a variety of options according to the therapeutic efficacy intended, and he described the scientific criteria needed for a proper selection.

Figure 3. *Disintegration test device described by Lewis (Source: Chemist and Druggist 1904)*

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A simpler experimental arrangement had already been described by Judd Lewis (1869-1959) in 1904. This author clearly saw the importance of readily disintegrating tablets and also anticipated the later concept of bioavailability: 'In judging the value of a tablet much importance must be attached to the readiness with which it will break up in the stomach – i.e., to the conditions under which it will become available physiologically.'[24] He suggested a simple device for standardized testing, consisting of a small funnel covered with a piece of muslin.

The tablet to be tested was fixed on the cloth by a spiral wire, and exposed to a solvent continuously dripping onto the tablet second by second (Figure 3). The 'time required for complete dissolution' should then be recorded. As a menstruum, tap water could be used, as could any other solution like artificial gastric juice. Within a single batch of products Lewis recorded rather constant values, pointing to some reliability of the method. Results for different brands varied, so that

> considerable differences between various brands of the same remedy are sometimes revealed. Some are very resistant, their surfaces scarcely broken after two or three hours continual action, while some of the soluble ones have entirely disappeared in a few seconds.[25]

Obviously, nothing had changed in the following decade, although the dosage form had already achieved a predominant place in daily practice. For example, in 1911, Seel and Friederich published extended investigations about the quality of tablets, also comparing industrial products with those extemporaneously prepared in pharmacies. They found many totally unacceptable analysis parameters, not only regarding disintegration times but also in relation to colour, weight and content, decomposition products, amongst others.[26]

In 1909 Blaschnek also reported the greatly varying disintegration behaviour of different tablets,[27] as did Dichgans investigating a couple of tablets containing acetylsalicylic acid.[28] In this study, five out of eleven tablets did not disintegrate within 24 hours in unstirred water at 20°C, while others decomposed in a few minutes. This clearly showed that at the beginning of the twentieth century quality assurance standards were urgently required.

Pharmacopoeial methods

Pharmacopoeias made a small but unassuming contribution to solving the tablet disintegration problem. The *Swiss Pharmacopoeia* of 1907 contained a short monograph entitled 'Pastilli compressi', stating that they should – when immersed in cold water – dissolve or disintegrate 'in [a] short time'.[29] The fifth edition of the *German Pharmacopeia* (DAB 5), issued in 1910, did not yet have its own monograph on tablets, but still subsumed them under 'pastilli', defined as 'drug preparations prepared from powdered substances by pressure or by transformation in a formable mass resulting in disks, tablets, cylinders, cones, spherical segments etc. and, if necessary coated with sugar, chocolate, glue, keratin or other substances'.

Compared to the earlier edition of the *German Pharmacopeia* (DAB 4), one sentence had been added, stating that 'pastilles […] must completely disintegrate in water at 37°C under occasional, gentle shaking within half an hour'.[30] This simple procedure was clearly far behind the scientific and technological state-of-the art of the time, in view of the fact that testing in artificial body fluids and other media had already been applied decades before.

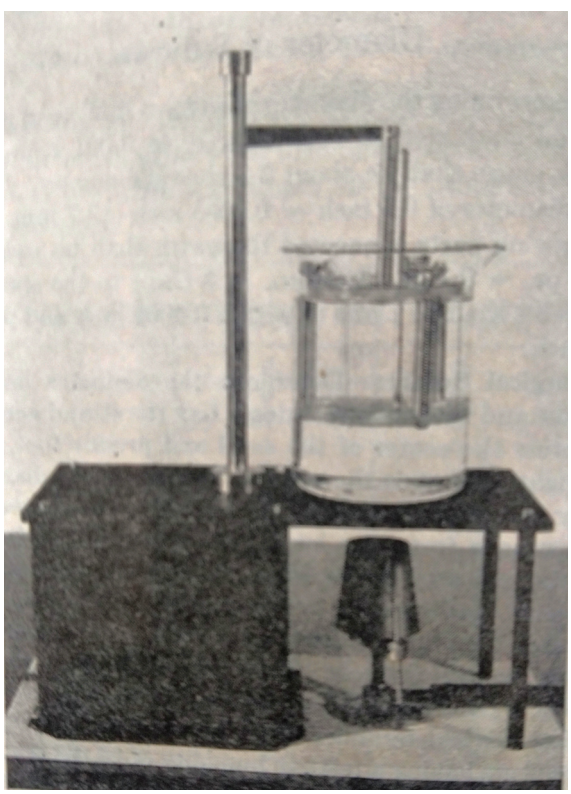

Figure 4. *USP 14 test apparatus (Source: United States Pharmacopoeia, 14th edition, 1950)*

Investigations published in 1911 found that 7 out of 28 tablets did not pass this simple test.[31] The sixth edition of the *German Pharmacopeia* (DAB 6) in 1926 contained a separate monograph about tablets, but did not give even the simplest test method any more. The same year, the *Brazilian Pharmacopoeia* introduced a formal

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requirement,[32] as did the *Belgian Pharmacopoeia* in 1930. The fifth edition of the Swiss pharmacopoeia gave a comparatively detailed disintegration test for tablets in 1933. One tablet was immersed in a 100ml Erlenmeyer flask with 50ml of water at 37°C under occasional gentle shaking. The tablet should have disintegrated or dissolved within 15 minutes.[33]

In the middle of the twentieth century, many major pharmacopoeias introduced disintegration tests for tablets. In Britain, this was done in the seventh addendum to the *British Pharmacopoeia* 1932 in 1945,[34] before the *United States Pharmacopeia* (USP XIV) set new standards in 1950. It firstly described the well-known 'basket-rack assembly' in detail (Figure 4).[35] Maximum time limits for the disintegration process were given in each tablet monograph, for example, 30 minutes for acetylsalicylic acid tablets.[36] Several other methods were available in the 1950s, still focused on disintegration times of solid dosage forms.[37]

From disintegration to dissolution

During the course of the 1950s, however, pharmacists more and more recognized the significance of the difference between disintegration and dissolution, as it became known that some 'tablets that disintegrated were nonetheless clinically inactive'.[38] So 'in the early 1950s it became clear that disintegration alone could not account for the physiological availability of drugs, and in many cases the dissolution rate was, instead, the limiting step'.[39]

This happened more than 50 years after the theoretical basis for dissolution experiments had been laid down by Noyes and Whitney[40] in 1897 and several others. But this was research which had been done by chemical engineering scientists, and had largely been neglected in pharmacy until the middle of the twentieth century.[41]

The turnaround was attributed to 'the fact that a new generation of pharmaceutical scientists were [sic] being trained to apply physical chemistry to pharmacy'.[42] Thereafter, knowledge about the influence of dosage forms on bioavailability increased substantially, as did the science of dissolution testing in general. These developments had tremendous significance in the evaluation and approval of generic drug products from the 1970s onwards.[43]

Conclusion

At the end of the nineteenth century, the dosage form of tablets revolutionized oral drug therapy. Being much more suitable for large scale production than any other dosage form, it contributed to the rapid development of the pharmaceutical industry on the one hand, and to the steep decline of extemporaneous manufacturing in pharmacies on the other. However, it gradually became obvious that a balance between sufficient robustness and appropriate disintegration properties of the tablets was crucial for their therapeutic value.

It seems that much more research had been devoted to production than to control procedures. This coincided with the traditional role of pharmacopoeias, which – at least until the second half of the nineteenth century – exclusively contained preparation methods rather than analytical procedures. There was also an historical perception that quality could be assured by detailed description of the production process rather than by *post hoc* analysis. Additionally, quality control in industry was still in its infancy, so that more or less uncontrolled products – promising high profit – reached the rapidly growing market.

It has been proposed that, in this situation, the pharmaceutical profession missed the unique opportunity to define its future role in securing the quality of industrially produced pharmaceutical products, so obviously transforming daily business.[44] In any case, the history of tablet manufacture and analysis is that of a learning process spanning several decades. In a first step, and in contrast to initial perceptions, it became clear that tablet manufacturing indeed needed several excipients, and that tablets did not necessarily disintegrate better than pills and pastilles.

Disintegration test systems were slowly advancing, until useful techniques entered major pharmacopoeias between the 1930s and the 1950s. Another important learning process led to the realization that the dissolution of tablets rather than their disintegration is crucial for bioavailability, a realization which was achieved by the integration of physical chemistry knowledge into the pharmaceutical sciences in the early 1960s.

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9. His almost exclusive knowledge, however, may have contributed to the commercial success of the tabloid preparations later marketed by the Burroughs, Wellcome company.

10. Burroughs, SM. (Note 8) 1877: 1-2.

11. Burroughs, SM. (Note 8) 1877: 5-6.

12. Burroughs, SM. (Note 8) 1877: 9-10.

13. Burroughs, SM. (Note 8) 1877: 10-12.

14. Burroughs, SM. (Note 8) 1877: 10-13.

15. These advantages had also been proposed in Germany before Burroughs did so by [Hager, H.] Trockene Arzneimittel in comprimierter Form. *Pharmaceutische Centralhalle für Deutschland*. 1874; 15: 361-363 or, from a medical point of view, Husemann, T. Pharmakologie und Toxikologie. *Jahresbericht über die Leistungen und Fortschritte in der gesammten Medicin*.1875: 9(1); 445-526, here 523.

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29. *Pharmacopoea Helvetica*, Edition Quarta. Bern, 1907: 330.

30. Deutsches Arzneibuch V 1910: 391. The definition clearly falls back behind Pharm. Helv. IV (Note 29), which had already separated compressed (Pastilli compressi) from ductile preparations (Pastilli). Relevant literature about the history of dissolution testing is neglecting these monographs issued in 1907 and 1910, erroneously stating that Pharm. Helv. V (1933) was the first pharmacopoeia considering the disintegration of tablets. So also did Dokoumetzidis, A. and Macheras, P. A century of dissolution research: From Noyes and Whitney to the biopharmaceutics classification system. *International Journal of Pharmaceutics.* 2006; 321: 1-11 as well as Schmid, K., Löbenberg R. Influence of the changed USP specifications on disintegration test performance. *Dissolution Technologies.* 2010: 6-10. This might be due to the fact that compressed powders were still regarded as 'pastilles' in pharmacopoeial nomenclature for a long time.

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32. This was not in fact the first one, as erroneously stated by Cartwright, AC. (Note 28) 2015: 71, most probably taken from Denston, TC., The standardization of tablets. *Journal of Pharmacy and Pharmacology.* 1954: 6; 1067-1073. It seems, however, that in the 1930s more and more national pharmacopeias started with simple tablet disintegration tests, including those of Switzerland, Denmark, France, Finlandand Russia. See Denston, TC. (this note) 1954: 1069.

33. *Pharmacopoea Helvetica,* editio quinta. Bern 1933: 259.

34. Cartwright, AC. (Note 28) 2015: 70.

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43. For this development see in particular Greene, J. *Generic. The Unbranding of Modern Medicine*. Baltimore, 2014.

44. For discussion see Hickel, E. Die Apotheker - Beruf der verpassten Gelegenheiten. Zweihundert Jahre Gewerbefreiheit und die Pharmazie. *Pharmazeutische Zeitung.* 1976: 121; 1185-1192.

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SHORT COMMUNICATION

Therapeutic stone powder from ecclesiastical sources: supplementary comments

Jan Weertz, Els Weertz and Christopher J. Duffin

Abstract

Consecrated earth or stone powder associated with churches dedicated to medieval saints, often of local significance, has particular importance in certain areas of Belgium and the Netherlands. Sources of supply range from the walls and other parts of the fabric of the church and earth from pilgrimage sites, to specially blessed ordinary building sand. The material has been – and often still is – employed in various ways by believers to increase agricultural success, to improve yield in animal husbandry, to preserve the health of livestock, to discourage vermin, and as a prophylactic and medicinal therapy for a range of conditions, often determined by special association with the saint in question.

Introduction

Pulverised rock material has been used medicinally since classical times. Jade, pumice, Irish slate, gypsum, clays, chalk, marls, and Fuller's Earth have all been exploited for their supposed healing properties, as have powders produced from fossil echinoid (sea urchin) spines and belemnites (to treat a wide range of diseases including kidney and bladder stones), and prehistoric stone axes (to treat epilepsy and to restore domesticated animals to full health). We have reported previously on the link between stone powders and various secular and ecclesiastical sources.[1]

The extraction of therapeutic powder by scratching the building stones of secular buildings such as town gates and town halls may be related to the ancient belief that the spirits of the deceased can inhabit localities associated with their deaths.[2] One of the consequences of town sieges was that death took place at town gates. Town halls were often sites where judges decided on the fates of prisoners. Thus, stones at these particular locations were more likely to be thought of as imbued with supernatural therapeutic power as a consequence of their formidable association with death.

The external walls and keystones of some medieval and renaissance churches, tombstones, and crosses, show systematically scratched surfaces as evidence of stone powder extraction, whose potential healing properties were reinforced by its consecrated origins. Powders from church building stones represent one extreme in a continuum of 'holy' source materials, ranging from earth obtained from sites of pilgrimage to the graves and dwelling places of (mostly medieval) saints. New evidence and additional information (see below) has become available since that initial work, prompting this brief update.

The stone powder extraction points include rows of deep, boat-shaped grooves; long, small and shallow grooves (as for example at Sankt Dionysiuskirche in the German town of Belm); and cup-shaped hollows. Cup-like impact sites of bullets and other projectiles can be distinguished from those worked for stone powder, but there are examples where impact sites have been later exploited for powder extraction. Similarly, overworking is indicated by cross-cutting relationships between different generations of grooves and cups. There seem to be regional trends in the style of scratch mark exhibited by church walls, probably a function of the type of building stone encountered as well, perhaps, as local traditions.

Distribution and numbers of locations

In our earlier article we cited the distribution of the scratch marks in the Netherlands, Germany and Belgium with further examples also being known from Britain and France. Further examples are now documented from Austria, Switzerland, the Czech Republic,

Figure 1. *Map showing the locations of the localities cited in the text. 1. Sint Gerlachuskerk, Houthem/St.Gerlach; 2. Sint Gerlachuskerk , Banholt; 3. Sint Catharinakerk, Montfort; 4. Goddelijke Zaligmakerkerk, Hakendover; 5. Sint Evermaruschapel, Rutten; 6. Saint Mortchapel, Haillot; 7. Camelitessenklooster, Vaals; 8. Heerle; 9. Onze Lieve Vrouw Tenhemelopnemingkerk, Prinsenbeek; 10. Woensdrecht; 11. Sint Gertrudiskerk, Vorst; 12. Lembeek; 13. Sint Ermelindiskerk, Meldert.*

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Denmark, Spain, Croatia, Italy, Norway, Poland, Rumania, Sweden, Slovakia, Egypt, Tunisia, Turkey, Israel and even Uzbekistan. Some yield only a few examples, whilst others have great numbers of them.[3] Over 210 locations displaying such scratch marks were recorded in our earlier contribution. Currently, we have found and visited more than 450 locations to verify the scratch marks they display, over 160 of which are located in the Netherlands and nearly 70 in Belgium.

Consecrated 'sand' and earth: register of sources

Often the consecrated 'sand' and earth have a relation with the saint or with his grave. Links between saints and healing have been forged over a long period of time, with special efficacy being credited to particular saints for particular diseases (usually related to an episode in the life of the saint), sites of pilgrimage, saintly relics, or memorials, amongst others.[4] People used to consume or use various parts of the body of a holy person. Pulverized bones ascribed to saints were seen as a very valuable medicine,[5] but understandably, it was not always easy to obtain the mortal remains of a saint.

People became satisfied with materials that had been in either direct or indirect contact with the saint in the belief that holy healing power had been subtly transferred. As substitutes and proxies they used gravestones or earth from the graves of the holy persons.[6] As time went on, it seems that church authorities both sanctioned this practice and introduced a more structured, 'official' approach to its enactment, as is clear from some of the examples in the list below. Also, this widening of application meant that earth from the graves of holy persons was extended to the use of general graveyard earth for its supposedly diverse curative and supernatural properties in the historical past.[7]

Current research has revealed the continued use of such materials today. A brief description of the results follows, and a map indicating the location of each place is presented in Figure 1.

1. Sint-Gerlachuskerk in Houthem-Sint

This church, located in the Dutch province of Limburg in Houthem-Sint Gerlach (in the municipality Valkenburg aan de Geul) is dedicated to the eponymous twelfth century knight, Gerlachus (born c.1100). A biography, the *Vita Beati Gerlaci Eremytae,* giving details of the legends surrounding this saint, was written around 1227.[8] It records how Gerlach, after having followed a military career, became a very pious Christian on the death of his wife. He undertook pilgrimages to both Rome (where he tended the sick for seven years) and Jerusalem. On his return to the Netherlands he gave up his possessions, became a hermit, and lived an extremely ascetic life of penance and austerity.

Gerlach is credited with having changed the water in a local well into wine on three separate occasions. Houthem, near Valkenburg in the southern part of Limburg, is where his original estate was located, and was the area to which he returned from his pilgrimage; it is now a regional centre of reverence dedicated to him. There is the tradition that, following his death in around 1170, numerous small miracles took place at his graveside. As a consequence, small amounts of soil were removed from his grave for therapeutic purposes in the belief that they were consecrated by the saint's presence.

This practice has taken on a more formal, structured pattern nowadays; consecrated limestone powder ('sand') is stored beneath the tomb of the saint (Figure 2) and made available to visitors for removal and use in the treatment of sick animals, mixed with corn to deter rats and mice, sprinkled in stables for the well-being of the cattle, and even added to the soil to improve crop growth. Indeed, the patronage of this particular saint is against plague and cattle diseases.

Figure 2. *The tomb of Saint Gerlachus equipped with the blessed 'sand' in Houthem-Sint Gerlach (the Netherlands).*

Figure 3. *Bags filled with blessed 'sand' in Sint Gerlachuskerk, Banholt (the Netherlands).*

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2. Sint-Gerlachuskerk in Banholt

This is another church dedicated to Saint Gerlach, and is located in the municipality of Eijsden-Margraten in the Dutch province of Limburg. Here, consecrated 'sand' is made available to the faithful once a year on Saint Gerlach's Feast Day (5 January); 150 small plastic bags are filled with 'sand' and deposited for collection around the statue of the saint at the back of the church (Figure 3). In this village, the 'sand' is believed to have special efficacy for the protection of cattle and other animals against sickness and disease; the material is thrown into the stables in the belief that it will keep the cattle healthy.

Figure 4. *Special bucket containing consecrated sand at Sint Catharinakerk in Montfort (the Netherlands).*

3. Sint Catharinakerk in Montfort

This church is located in the municipality of Roerdalen in the Dutch province of Limburg. Saint Anthony the Great (c.251-356) was an Egyptian Christian monk, the details of whose life were recorded around 360 by Athanasius of Alexandria (c.296-373), a prominent theologian, author and Bishop of Alexandria.[9] Anthony's remains, originally buried on the mountain on which he lived, were transferred to Alexandria in 371, and from there to Constantinople for their protection from the invading Saracens. Then, during the First Crusade in the eleventh century, they were given to Joscelin of Courtenay, Count of Edessa (died 1131) who took them to Saint-Antoine-l'Abbaye (in the Departement Isère, southern France).

There, the relics were associated with various miraculous cures, particularly of ergotism, which came to be known as 'St Anthony's fire'. The Sint Catharinakerk reveres St Anthony. In the church, sand (purchased from local builders' merchants) is placed in a bucket next to his statue (Figure 4). Parishioners and visitors are able to take the material, which is applied to the fields to increase fertility and, as with 'sand' associated with St Gerlach, used to protect cattle from sickness.

Figure 5. *Store of consecrated earth at Hakendover (Belgium).*

4. Goddelijke Zaligmakerkerk in Hakendover

The town of Hakendover lies to the southeast of Tienen in the Belgian province of Flemish Brabant. The town is well known because of its annual 'paardenprocessie' (horse procession) which takes place on Easter Monday. This involves the blessing of both pilgrims and animals by the priests, followed by a horse race over the fields. Pilgrims are permitted to take samples of the blessed earth from the cemetery that surrounds the church. The earth is used to protect against all kinds of evil and disaster. It is also thrown onto the fields and mixed with cattle feed. A supply of the earth is stored ready for collection in a roofed construction at the rear of Goddelijke Zaligmakerkerk (Figure 5).

5. Sint Evermaruschapel in Rutten

This chapel is located in Rutten (municipality of Tongeren) which lies in the Belgian (Flanders) province of Limburg. In the village, the Sint Evermaruschapel has a small pit in the floor of the nave, just in front of the altar (Figure 6). The pit is covered with a removable stone tile (Figure 7). The pit houses a fine-grained, powdery consecrated earth which is made available to visitors for removal. It is commonly added as a curative to the food of sick animals, as well as being thrown onto the fields to aid fertility. Believers in the efficacy of the earth also use it themselves against various diseases and discomforts; local people claim that it is beneficial for nearly every condition imaginable; one anecdote tells of the earth being particularly effective against polyps.

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Figure 6. *Location of the tile-covered pit just in front of the altar in the nave of Sint Evermaruskapel, Rutten (Belgium).*

Figure 7. *Detail of the tile-covered pit (Sint Evermaruskapel, Rutten).*

Some place a sample in a small bag and keep it under the pillow at night. The caretaker of the pit obtains the earth from the meadow surrounding the chapel. Before it is consigned to the pit, the earth is sieved and any small stones are removed. The church/chapel reveres a seventh century Frisian pilgrim, St Evermarus who, along with his seven companions, was murdered by bandits at Rutten whilst they were resting after their return from a pilgrimage to Santiago de Compostella in Spain. According to legend, the nobleman Pippin von Herstal (c.635-714) came across the bodies during one of his hunting trips, and had the corpses buried. Evermarus was canonised in 968, and a wooden chapel was built in the meadow where his remains were discovered, later (1784) replaced by a stone church.

Figure 8. *The altar at Saint Mortkapel, Haillot (Belgium). Note the cavity beneath the altar where the consecrated earth is kept, plus the presence of a large stone, perhaps a menhir or standing stone.*

6. Saint Mortchapel in Haillot

Haillot is a village in the municipality of Ohey which lies in the Belgian (Wallonia) province of Namur. It contains the fifteenth century chapel of Saint Mort ('the dead saint'). Apparently, a monk from Saint-Laurent near Saint-Trond called Gérard de Gingelom visited the church in 1466 and enquired about the saint. The information which he gathered was recorded in a manuscript now held in the Royal Library, Brussels.[10] It tells of a woman from Antvalle (now called Andenelle) who presented her stillborn child to the Virgin Mary de la Vignette at Huy on the River Meuse, whereupon the child was quickened; it was baptised with the name 'Death'. When he grew up, the child lived the life of a hermit. At the death of his parents he gave all that he had to the poor, dedicated his life to the service of God and was well loved. Diabolically inspired bandits killed him for the riches they supposed he was hiding.

The women of Andenne determined to collect his body and take it to their church, but when the remains were loaded onto a cart, the horses could not be persuaded to move. Left to their own choice, the horses carted the body via a circuitous route over tracks and through the countryside to the church where the Saint had originally been baptised. There, he was buried between two pillars and his grave became a shrine at which many miracles of healing were attested, especially of gout, toothache and other diseases.

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Visitors take the consecrated earth from a cavity under the altar (Figure 8) and add it to animal feed to preserve the health of their livestock; it is said that cows which have eaten the earth give a higher milk yield. Godefroid Petit, a priest of Saint-Mort in the middle of the sixteenth century, relates that all sorts of *ex voto* offerings were left there by visiting pilgrims. Even today, the pit is littered with children's dummies left as votive offerings by those seeking ease for their children's toothache.

Consecrated 'sand' and earth in the recent past

The use of sand and earth existed in the recent past at various locations, which include the following:

7. **Karmelietessen Klooster in Vaals**: Vaals lies in the extreme southeast of the Dutch province of Limburg. In the past the monks from the Karmelietessen Klooster (Convent of the Carmelites) sold stone powder as a medicine. Unfortunately, the convent no longer exists.
8. **Heerle**: In the town of Heerle (municipality of Roosendaal in the Dutch province of North-Brabant) parishioners were able to obtain specially blessed white sand up to the end of the last century. This so-called 'Gertrudissand' was used as a pesticide to discourage mice and rats.
9. **The Onze Lieve Vrouw Tenhemelopnemingkerk in Prinsenbeek**: In Prinsenbeek (municipality of Breda in the Dutch province of North-Brabant) there is a further association (see Heerle, above) between Saint Gertrude of Nivelles (c.621-659) and pesticidal sand. According to legend Saint Gertrude lived in Prinsenbeek and when rodents spoiled harvest, she helped them to rid the town of them.
10. **Church in Woensdrecht**: Here, in the Dutch province of North-Brabant, specially blessed 'Gertrudissand' was available for collection on 17 March (the anniversary of her death) from a bin standing at the back of the church.
11. **Sint Gertrudiskerk in Vorst**: In Vorst (in the province of Antwerp in Belgium), supplicants not only asked Saint Gertrude for help against vermin, but also to cure wounds on the nose and the lips and to get rid of eczema. It was also thought that Gertrude could help in cases of mental illness and seduction by the devil. It was also believed that Gertrude could help in times of ravaging by plague or other epidemic diseases. Pilgrims collected earth from the cemetery for a wide range of applications.
12. **Church in Lembeek**: Saint Veronus of Lembeek or Saint Vroon (died 863) is worshipped in Lembeek (in the municipality of Halle in the province of Flemish Brabant in Belgium). The saint's assistance was sought for a variety of diseases including headaches, meningitis and fever. In the past pilgrims removed and bagged earth from a pit at the grave of the saint. The bag was then laid under the head at night in order to effect a cure. The pit was later closed but pilgrims were able to collect bags of earth from the church itself
13. **Sint Ermelindiskerk in Meldert**: The church of Saint Ermelinde in Meldert (municipality Hoegaarden in the province Flemish Brabant in Belgium) is dedicated to the sixth-century hermitess, Ermelinda (510-590), who was very charitable to the poor, set up a hermitage in the area, and died in the town. According to legend, the staff of Saint Ermelinde sprouted into a thorn bush next to the church; parishioners collected the earth from around the bush for therapeutic purposes and agricultural blessing.

Conclusion

It is clear from the discussion above that stone powder derived from a range of ecclesiastical sources, usually tied to pilgrimage centres associated with a range of medieval saints, enjoyed considerable local popularity in Belgium and the Netherlands. Whilst the list of localities where 'sand' and earth are still used for medical or magical purposes today – or were used in the recent past for this goal – is somewhat limited, further research may yield even more examples.

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